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Feed-associated colitis of growing pigs and its interaction with enteric infections

Colite nutricional em suínos de crescimento e sua interação com infecções entéricas

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INTRODUCTION

Colitis is a common cause of diarrhoea in growing pigs in all countries. It is a major cause of financial loss to pig farmers due to delays of up to 14 - 21 days in pigs attaining finishing weight and increased mortality. The physiological causes of diarrhoea in pigs, the pathogens involved, the parts of the intestine that they affect and their prevalence by age of pigs has been described [40]. In broad terms, the causes can be divided into the following categories; infectious causes (bacterial, parasitic and viral agents), feed/diet associated causes (non-starch polysaccharides, niacin deficiency) and colitis associated with immunosuppressive disease e.g. postweaning multisystemic wasting syndrome. *Brachyspira* (*B.*) *hyodysenteriae* and *B. pilosicoli* are known to occur commonly in pig herds with diarrhoea problems in southern Brazil [2]. For veterinarians, with training primarily focussed on infectious diseases, this tends to be our first thought when considering the cause of diarrhoea and colitis in pigs. However, there is increasing awareness of the role of non-infectious factors based on commercial situations where no infectious causes were detected, where pathological lesions were nonspecific and where infectious disease control strategies failed to bring about any improvement. When non-infectious factors and infectious diseases are present in combination, this gives rise to complex situations that require the best diagnostic skills and knowledge of the veterinarian. This paper focuses on some of the feed/diet-related factors that have been shown to be associated with diarrhoea and colitis in growing pigs. The studies that have involved the interaction between dietary factors and infectious agents are also reviewed and discussed.

DIETARY FACTORS

Niacin/Corn

It is a surprise to many veterinarians that diet-associated colitis was recognised more than 50 years ago in pigs fed corn-based rations with limited protein supplementation [3, 22]. Affected pigs had poor growth rates, diarrhoea and anaemia associated with chronic colitis. The colonic mucosa was darkly congested and mucosal necrosis with multifocal ulcers were present. The condition was attributed to deficiency of tryptophan. Niacin supplementation of the diet prevented the condition and brought about recovery in affected pigs. Deficient diets had less than 15 ug/g niacin content. Although this form of colitis is unlikely to happen in pigs fed a commercial compound ration or a home-mix ration with adequate protein and vitamin/mineral supplementation, it is worth remembering in situations where pigs are fed a very basic carbohydrate diet or where 'alternative' diets that are protein-deficient are used.

Non-starch polysaccharides/Wheat, Barley and other cereals

In the late 1980's, a diarrhoea problem apparently associated with feed emerged on many farms in the UK and other European countries, the USA and Canada [15,29,33]. It affected successive batches of growing pigs

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between approximately 12–40 kg bodyweight, with up to 80% of the batch obviously affected. The condition could not be attributed to any infectious agents but it showed a clear association with feeding certain pelleted diets [30]. A series of farm-based trials aimed at further characterising the condition showed a clear association with diets high in wheat that were pelleted at high temperature. It could be prevented by either feeding the diet as a meal (avoiding high temperature processing) or by adding arabinozylanase to the ration before it was pelleted [36]. The hypothesis was that diets with high levels of non-starch polysaccharides (NSPs), both insoluble and soluble were capable of causing diarrhoea and colitis in pigs. The term 'nonspecific colitis' was given to the condition because of the absence of pathogens and the lack of any unique pathological features. This is a poorly descriptive term for the condition but no better name has emerged as yet.

Factors in wheat thought to be associated with nonspecific colitis relate to the variety ('hard' or 'soft') and the presence of the 'Rye gene' (1B1R translocation) [M. Hazzledine, personal communication]. The Rye gene translocation was introduced a number of years ago to improve yield and yellow rust resistance. The 'hard' varieties of wheat, particularly those containing the 'Rye gene' (e.g., Slepjner, Gladiator, Napier, Glasgow, Savannah, Tanker and Welford) not only have inferior feeding quality for pigs but also present the highest risk of nonspecific colitis [M. Hazzledine, personal communication].

The total fibre values of feedstuffs (defined as NSPs plus lignin) is said to be vastly underestimated when assayed as crude fibre [24]. As a general rule, the total fibre in ingredients such as maize, rice bran or wheat bran/pollard is more than three times the amount indicated by the crude fibre measurement, for example, maize contains 2.5% crude fibre, but actually contains 10% total fibre; wheat by-products contain 8–11% crude fibre, but in reality contain 30–40% total fibre [24]. The processes associated with digestion of high levels of fibre in the colon by bacteria are thought to cause the adverse effects that result in colitis. Factors such as the chemical nature of the plant fibre, the solubility and degree of lignification influence the speed and extent of degradation of the fibre polysaccharides in the large intestine. Beta-glucan, soluble factors and pectins get degraded fairly rapidly in the caecum and proximal colon [1,4,11]. The more insoluble fibre types such as cellulose and insoluble arabinoxylans are degraded more slowly in the more distal sections of the colon [1,11]. The ultrastructural changes found in the colon at the early stages of diarrhoea in NSC cases are loss of microvilli and apoptosis of surface epithelial cells [36]. The cause of these changes is not understood but increased concentrations of potentially toxic components such as ammonia, indoles and phenols arising from increased bacterial fibre degradation offer a possible explanation.

EPIDEMIOLOGICAL STUDY INTO RISK FACTORS IN NONSPECIFIC COLITIS

To determine the major epidemiological associations or risk factors associated with non-specific colitis on commercial units, a case-control study was carried out on 17 farms with NSC and 10 control farms [5,32]. The aim was to provide advice on management factors that reduce the risk of non-specific colitis that could be implemented on farms with this problem. Approximately 80 potential management and dietary factors were analysed. The strongest and most significant associations for NSC were dietary factors most notably higher non-starch polysaccharide levels in grower diets (especially those with higher composition of glucose, xylose and arabinose) (Table 1). The mean percentage of wheatfeed was almost five times higher in the grower diets of NSC farms as compared with control farms. Although the study highlighted a number of other trends concerning weaner and grower diets, the NSP content of the grower diets was the only factor that emerged as being statistically significant. Home-mix rations were generally protective especially when fed as a meal and there was a greater tendency for NSC-affected units to use pelleted diets. Zinc oxide medication in the weaner ration and/or inclusion of antibiotic growth promoters in the weaner ration were protective which could relate to controlling the balance of flora in the hindgut.

Table 1. Non-starch polysaccharide constituent sugar content (g/100g feed) of pig grower diets used on 17 farms with nonspecific colitis (NSC) and 10 control farms with no diarrhoea or colitis (Control).

Sugar*	NSC	Control	SED	P
Rhamnose	0.21	0.13	0.042	0.06
Fucose	0.03	0.05	0.019	0.30
Arabinose	2.21	1.66	0.136	**<0.001**
Xylose	3.49	2.62	0.187	**<0.001**
Mannose	0.32	0.18	0.072	0.06
Galactose	1.18	1.10	0.051	0.10
*Glu*cose	4.41	3.14	0.230	**<0.001**
GlcA	0.06	0.05	0.032	0.79
GalA	0.72	0.50	0.082	0.01
Total	**12.68**	**9.42**	**0.461**	**<0.001**

*Diets were analysed for non-starch polysaccharide content as previously described [9].

P: Statistical comparison using one-way analysis of variance.

Source: [32].

Of the management-related variables, only a few significant associations were identified namely higher numbers of pigs per pen and fan ventilation in the weaner and grower accommodation. This suggested that NSC tends to be associated with the more intensive systems of weaner production. However other factors such as higher humidity and ammonia levels possibly associated with fan ventilation could be stress factors that play a contributory role, such as altering the balance in the intestinal flora. This will be discussed further under the role of the microflora in expression of colitis.

Interventions for dietary causes

Although nonspecific colitis can be controlled by feeding meal as opposed to pellets or ensuring the dietary ingredients are low in NSPs, there are commercial reasons that make such measures impractical. These include feeding systems that block if meal is used, commercial experience of better growth and production with pelleted feeds in general and the expense and unreliability of sourcing specialist ingredients such as cereals low in NSPs. Instead, the potential control measures that have been studied included reducing the level of wheat in favour of barley, including an enzyme or a combination of enzymes in the ration, or including betaine in the ration. The enzyme products were selected on the basis of previous work that showed potential in smaller scale trials. Betaine was included as it is reputed to have a protective effect on intestinal epithelium. The possibility of it protecting the colonic microvilli and preventing apoptosis merited exploration. These studies were carried out in two large trials using commercial pigs fed on a ration that had consistently caused nonspecific colitis in pigs on the source farm [37]. The ration is denoted a provocative pelleted grower ration. The results of two trials are presented here.

Trial 1 comprised four treatments namely (1) pigs fed the provocative pelleted grower ration (PGR) (group w) (2) pig fed the PGR with wheat replaced by 50:50 wheat:barley (group b) (3) pigs fed the PGR as meal (non-pelleted) (group m) (4) pigs fed the PGR supplemented with 4000ug/kg beta-xylanase (group p).

Trial 2 also comprised four treatments namely (1) pigs fed PGR (group w2) (2) pigs fed PGR supplemented with 2550 ug/kg beta-gluconase and 6120 ug/kg beta-xylanase (group g2) (3) pigs fed PGR supplemented with 4000ug/kg beta-xylanase (group p2) (4) pigs fed PGR supplemented with 2 kg/tonne betaine (group b2)

For each trial batches of 320 weaners (approx. 16 kg) from a 'high health' status farm with a history of nonspecific colitis were divided into four groups, each comprising four pens of 20 pigs per pen. Pre-trial testing of pigs showed no evidence of enteric pathogens. Each group was fed the respective trial diet *ad libitum* for 20 days. Diarrhoea scores per pen on a scale of 0 – 10 were recorded daily according to pen faecal consistency and the number of pigs with diarrhoea (0=no diarrhoea, 10=all visible faeces diarrhoeic and >50% of pigs per pen with diarrhoea). Data were analysed by non-parametric statistics for significance of difference between medians (Kruskall Wallace test). Weight gain and feed usage on a pen basis were tested by analysis of variance. Faecal and post mortem monitoring for enteropathogens was performed.

In trial 1 all pens showed an increase over time in diarrhoea score with pigs in groups w and b showing more diarrhoea than those did in the other two groups. Pigs in group m showed little evidence of diarrhoea and had the lowest scores overall (Figure 1). Diarrhoea score showed highly significant treatment effect with all groups differing significantly from each other after 6 days on the diets. There was no significant difference in daily gain between groups but feed conversion ratio (FCR) was significantly poorer in group b than group m and p, with group w being intermediate (P=0.018). There was a significant (P=0.009) positive correlation between FCR and mean clinical score (poorer FCR associated with higher clinical score).

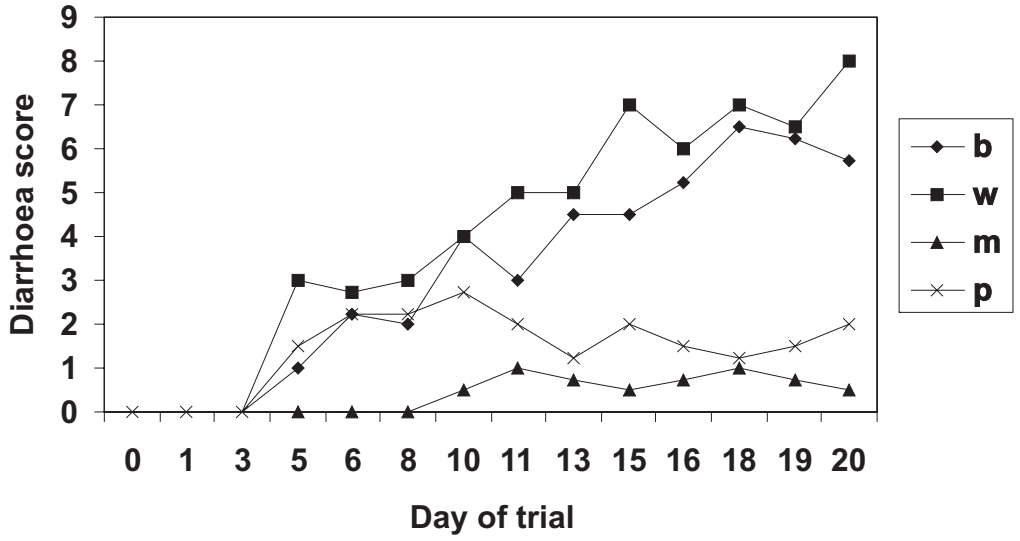

Figure 1. Trial 1. Dietary intervention study for the control of nonspecific colitis in commercial pigs.

The chart shows the median diarrhoea scores for pigs in each of four trial groups, in relation to days on dietary treatments, using the scoring system described in the text. Highly significant differences between all groups occurred after day 6 of the trial. Each group was comprised of 80 pigs with the following dietary treatments:

Group w: the provocative grower ration (PGR) pelleted.

Group b: the PGR with wheat replaced by 50:50 wheat:barley, pelleted.

Group m: the PGR fed as a meal (not pelleted).

Group p: the PGR supplemented with 4000 ug/kg beta-xylanase, pelleted.

Source: [37].

In trial 2, all groups showed an increase in diarrhoea score over time and the treatments diverged significantly after 7 days on the diets (P<0.001). Diarrhoea scores for the w2 and b2 groups continued to increase, group g2 was the lowest and p2 stabilised at slightly above g2 (Figure 2). There was no significant difference in daily gain between groups but FCR was significantly poorer in groups w2 and b2 than groups p2 and g2 (P<0.001). There was a significant positive correlation between FCR and mean diarrhoea score (P<0.001) with poorer FCR associated with higher clinical score. No bacterial enteropathogens were detected in diarrhoeic samples or from pigs examined PM in either trial. Any deaths that occurred were all accidental in nature.

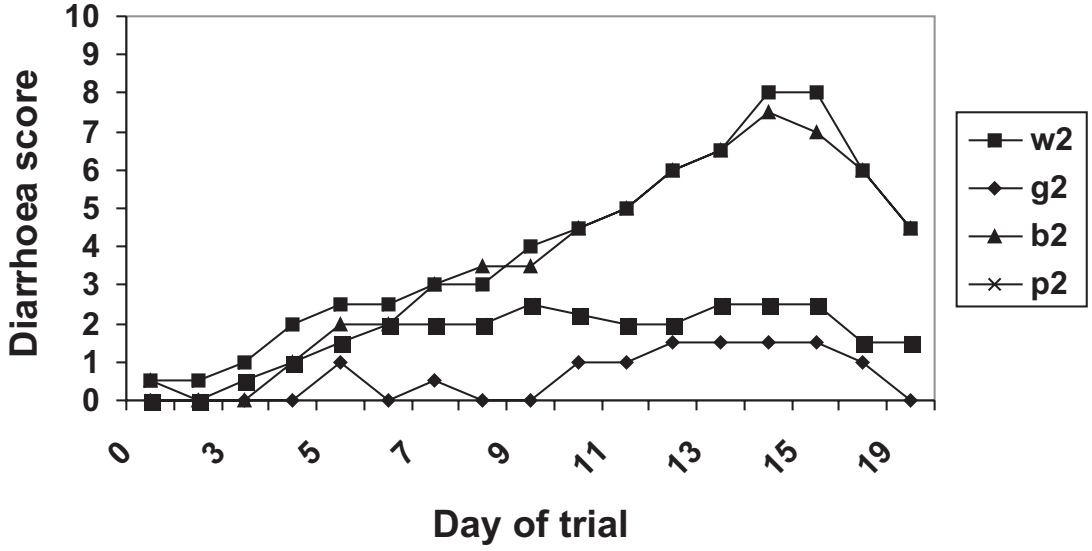

Figure 2. Trial 2. Dietary intervention study for the control of nonspecific colitis in commercial pigs.

The chart shows the median diarrhoea scores for pigs in each of four trial groups, in relation to days on dietary treatments, using the scoring system described in the text. Highly significant differences between all groups occurred after day 7 of the trial. Each group was comprised of 80 pigs with the following dietary treatments:
Group w2: the provocative grower ration (PGR) pelleted.
Group g2: the PGR supplemented with 2550 ug/kg beta-gluconase and 6120 ug/kg beta-xylanase, pelleted.
Group b2: the PGR supplemented with 2 kg/tonne betaine, pelleted.
Group p2: the PGR supplemented with 4000 ug/kg beta-xylanase, pelleted.
Source: [37].

In conclusion nonspecific colitis was associated with poorer FCRs in both trials. Inclusion of beta-xylanase or beta-xylanase and beta-gluconase combinations in the pelleted diet, or meal feeding had beneficial effects in controlling nonspecific colitis. The improved FCR values for the enzyme-supplemented groups in Trial 2 could in-part be attributed improved energy availability from diets resulting from better break-down of by-products by enzymes and hence, better utilisation of dietary ingredients [24]. Inclusion of betaine in the diet or replacement of the wheat component with 50:50 wheat:barley were not found to be protective in these trials.

THE INTERACTION BETWEEN DIET AND INFECTIOUS COLITIS

Most of the research into the interaction between diet and infectious colitis in pigs has involved swine dysentery. However, understanding has been confounded by the inconsistency of results achieved by different groups. Whereas a highly digestible cooked rice diet was found to be protective in some studies [28] it was not in others [19,20]. Feeding the cooked rice diet to pigs already affected with swine dysentery did not reduce the duration or severity of disease [8]. In a study of different cereal types, feeding steam-flaked maize or sorghum reduced the incidence of the disease [25]. Soluble NSP and resistant starch were identified as important factors promoting large intestinal fermentation and bacterial colonisation whereas with the addition of a source of mainly insoluble NSP (oat chaff) the diet remained protective [26]. Addition of enzymes to wheat based diets or the use of heat extrusion to increase digestibility of starch in the small intestine were tested in terms of their potential protective effects in swine dysentery but neither processes prevented colonisation [8]. Likewise the use of a sorghum based diet was tested as sorghum is inherently low in soluble NSPs but this diet was not protective against swine dysentery [8]. However, the particle size of diets (grind size or grist size) was important; with significantly more pigs developing swine dysentery with coarsely ground wheat or sorghum than with these grains finely ground [13]. More recent work has shown that high levels of soya bean meal promote the onset of swine dysentery [18].

In porcine colonic spirochaetosis caused by *Brachyspira pilosicoli*, pigs on the cooked rice diet developed infection later and to a lesser extent than pigs on a wheat-based diet [12,21]. In a study to investigate the effects of dietary changes on pigs with naturally-acquired *B. pilosicoli* infection, significant improvements were recorded in the clinical signs, faecal consistency (measured as % faecal dry matter), growth rate and the intestinal retention time in

pigs fed on a barley-based ration with low NSP content as compared with the wheat-based rations fed as standard on the source units [38]. The comparative data for the mean intestinal retention times for normal pigs and pigs with porcine colonic spirochaetosis fed the two respective diets is shown in Table 2. A significant positive correlation was recorded between the mean intestinal retention time and growth rate in pigs with porcine colonic spirochaetosis. The latter studies showed a clear role for diet in the expression of clinical signs and physiological changes in porcine colonic spirochaetosis.

Table 2. Mean intestinal retention time in normal pigs and pigs with porcine colonic spirochaetosis (PCS) from 6 farms fed two different rations. Intestinal retention times were measured on day 12 of trials.

Farm	Mean intestinal retention time (hours)			
	Farm's ration*		Test ration	
	Normaln=2	PCSn=6	Normaln=2	PCSn=6
1	24.1	20.3	30.7	27.8
2	25.0	18.9	32.5	26.2
3	26.6	21.8	33.0	28.5
4	29.4	22.3	31.9	29.3
5	24.4	19.8	27.5	25.2
6	27.0	21.5	29.8	27.2
Average	26.1	20.8	30.9	27.4

*commercial compound wheat-based rations fed as standard on the respective farms; ^ barley-based ration with low NSP content. Other than NSP content, the Test ration was formulated to the same specification as the respective parallel diet.
Source: [38].

Another infection that can be influenced by dietary effects is salmonellosis. Recommended control measures for salmonellosis in commercial farms include the feeding of meal instead of pellets as this is known to reduce the sero-prevalence levels in finishing pigs tested by meat-juice ELISA [6]. In a further intervention study, it was shown that herds using pelleted feeds could reduce the salmonella sero-prevalence by mixing 25% non-heat treated, non-pelleted wheat or barley to the diet [7]. The basis for the improvement is not understood but presumably it is through the reduction in colonisation potential of salmonella. Studies carried out to investigate this further showed that feeding meal resulted in increased viscosity of stomach contents as compared with pelleted feed [14]. A higher content of organic acid producing lactobacilli and a higher concentration of organic acid in the meal-fed pigs were thought to result in a reduction of coliform numbers including salmonella [7].

In contrast to salmonellosis, colonisation of the colon by *Trichuris suis* did not appear to be affected by diet [34]. Worm counts were lower in pigs fed a diet of fermentable carbohydrates as compared with a diet supplemented with resistant carbohydrates but the differences were not significant. Interestingly though, morphological differences were recorded in the pigs fed the different diets. Those fed the diet supplemented with resistant carbohydrates had larger crypts, both in terms of area and height, and a larger area of mucin granules within crypts as compared with the pigs fed the diet supplemented with fermentable carbohydrates [34]. In a subsequent three-factorial trial by this Danish group, the effects of diet were compared in pigs challenged with a combination of *B. hyodysenteriae* and *Trichusis suis* [35]. Both diets were based on triticale and barley but one was supplemented with rapeseed cake (Diet 1) while the other was supplemented with highly fermentable carbohydrates comprised of dried chicory roots and sweet lupins (Diet 2). Whereas 94% of the pigs on Diet 1 developed signs of swine dysentery and shed infection, none of the pigs on Diet 2 developed disease. *T. suis* infection occurred in pigs on both diets. Pigs on Diet 1 that were challenged with both pathogens showed signs of swine dysentery for longer than pigs that were challenged with *B. hyodysenteriae* alone [35]. The most interesting finding was that pigs were apparently completely protected against developing swine dysentery when fed a diet supplemented with dried chicory and sweet lupins. This will be discussed further in the following section on the colonic microflora and infectious colitis.

THE ROLE OF THE COLONIC MICROFLORA IN THE EXPRESSION OF INFECTIOUS COLITIS AND INFLUENCES OF DIETARY FACTORS

Previous studies have shown that a diverse colonic microflora is necessary for *B. hyodysenteriae* colonisation [39]. However little is known about the microbial interactions or conditions that promote infection. In an in-depth microbiological study the major classes of the colonic microflora were compared between healthy pigs, pigs with nonspecific colitis and pigs with swine dysentery or porcine colonic spirochaetosis [31]. Compared with the healthy pigs, pigs that were affected with any of the forms of colitis showed a significant reduction in total anaerobes, *Bacteroides, Eubacterium* and *Fusobacterium* species. Additionally decreased numbers of total aerobes and aerotolerant lactobacilli were recorded in the affected groups. As so little is known about the pig's colonic microflora and its role in disease, it is uncertain whether the differences reported would predispose to colitis and if so, what measures could be taken to prevent significant imbalances developing.

As part of the Danish three-factorial study described under studies on infectious colitis [35] an analysis of the microflora was carried out on pigs fed the different diets [23]. Using terminal restriction fragment length polymorphism (TRFLP) on colonic contents, pigs fed the diet supplemented with chicory roots and sweet lupins were found to have a higher proportion of *Bifidobacterium thermoacidophilum* and *Megasphaera elsdenii* that might have inhibited the colonisation of *B. hyodysenteriae*. Growth of bifidobacteria is selectively promoted by feeding chicory-derived fructans [27] and bifidobacteria produce bacteriocides that are inhibitory to certain pathogenic micro-organisms [10].

The effects of feeding diets with different NSP levels on the enteric microbial populations was studied in cannulated pigs [16]. Using TRFLP and biochemical fingerprinting, differences were recorded in the total gut microflora and coliform diversity with diets of different NSP content. Further research is required to understand the implications of these changes.

The possibility of nutritionally-induced immunoregulatory control of infectious colitis in pigs was studied through dietary supplementation with conjugated linoleic acid (CLA) [17]. Pigs fed a CLA-supplemented ration from a few days before oral challenge with B. hyodysenteriae and continuing through to the end of the trial, did not show clinical signs or pathological lesions of swine dysentery despite the organism being isolated from all challenged pigs. In contrast, pigs fed a soybean-oil supplemented diet showed normal disease expression and reduced growth rates as compared with the CLA-supplemented pigs [17]. The findings suggest that CLA modulates the pig's immune effector mechanisms instead of directly targeting the bacterial agent and offers an alternative approach to the control of infectious colitis.

CONCLUSIONS

This paper addresses several complex issues surrounding porcine colitis, highlights some results of recent research and indicates areas for further study. Currently, successful control of infectious colitis depends upon the correct diagnosis and targeted intervention using methods such as strategic administration of an effective antimicrobial agent coupled with suitable management practices. The effects of a range of dietary intervention measures for NSC and infectious colitis have been reviewed. Currently, there is only limited understanding of the key factors but some important indicators are emerging that could form the basis of control measures in the future. The majority of promising interventions have not been assessed under commercial conditions so field trials are required to confirm their practical value. Not only is NSC an important performance-limiting condition but pigs with NSC could have an increased susceptibility to infection by large intestinal pathogens. The mucosal erosions and inflammatory damage associated with NSC are lesions that are likely to promote tissue colonisation and invasion by bacteria. Consequently, pigs with NSC are thought to be at added risk of developing enteric pathogenic infections, thereby adding to the economic consequences of these diseases. Understanding the basis of feed-related colitis and methods to prevent it are of importance to pig health and production. Veterinarians, nutritionists and cereal chemists should collaborate to improve understanding of how and to what extent different cereal types and nutritional supplements effect the colonic physiology of the pig, including the balance of the microflora and predisposition to infectious colitis. Defining the circumstances under which dietary intervention measures could be used to prevent colitis, and establishing the best procedures in relation to the variables involved, would be highly beneficial for the pig industry in the future.

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