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Development of antibiotic resistance and options to replace antimicrobials in animal diets

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As there is a risk of developing antibiotic resistance, a number of commonly-used antimicrobial growth promoters have been banned in the EU member states. This decision has put new emphasis on using the diet to control enteric bacterial infections of pigs. Dietary carbohydrates constitute a major proportion of diets for pigs, and the carbohydrate fraction has a diverse composition, with different properties in the gastrointestinal tract, some of which are of importance to gut health. Findings from different studies indicate that dietary carbohydrate composition influences the expression of swine dysentery and infection with nematode worms after experimental challenge with *Brachyspira hyodesenteriae* and *Oesophagostumum dentatum* respectively. In both cases the type, amount and physico-chemical properties of the carbohydrates entering the large intestine played an important role in the infection, and emerging data suggest a synergism between different porcine pathogens. There is also increasing evidence that the feed structure, which relates to the type of plant material in the diet and the way it is processed, can be used to reduce *Salmonella* prevalence at the herd level. However, it should be stressed that using the diet to manage gut health is not straightforward, since the expression of a pathogen in many cases requires the presence of other components of the commensal biota.

Pigs: Antibiotic resistance: Carbohydrates: Bacteria: Parasites

Antibiotics have been used in animal production for many years for therapy, as a prophylactic against bacterial infection and as antimicrobial growth promoters (AGP). It is generally accepted that all use of antibiotics may potentially result in antibiotic residues in the tissue of treated animals, but in recent years the greatest concern has been about the heavy use of antibiotics as growth promoters. Long-term use of AGP may select for the survival of resistant bacteria and strains, which then may be transferred to other bacteria, thus making them resistant (Aarestrup, 1999). As a result of the risk for transmission of antibiotic resistance from food animals to man, Sweden formulated a national strategy for animal production without the use of AGP in 1986 (Wierup, 1996). In May 1995 the Danish government banned the use of avoparcin, which was followed by similar national actions taken by Norway and Germany, and from 1 April 1997 avoparcin was banned in all EU member states. In December 1998 the EU Council of Ministers decided to ban the use of virginiamycin, tylosin phosphate, spiramycin and zinc bacitracin in animal feedstuffs from 1 July 1999 (Wegener *et al*. 1999).

The actions taken by national bodies and the EU have reduced the total use of antibiotics in pig production. However, Danish experience suggests that more emphasis has to be put on the development of better feeding and management strategies to limit enteric bacterial infections in pigs. The focus of the present paper will be on the possibility of dietary management of the physiology of the gastrointestinal tract, with special emphasis on the use of dietary carbohydrates to reduce infectious diseases of the gut.

Abbreviations: AGP, antimicrobial growth promoters; NDO, non-digestible oligosaccharides; RS, resistant starch; SCFA, short-chain fatty acids; VRE, vancomycin-resistant *Enterococcus faecium.*

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Development of antibiotic resistance

It has long been known that supplementing the feed of food animals with AGP increases performance and helps to control diseases. A review by Armstrong (1986) concluded that the use of AGP improved live-weight gain by 5–6 % and feed conversion efficiency by 3–4 %, with the most pronounced effects observed in young animals. The mechanisms by which AGP act are not clear, but various mechanisms have been proposed. First, the nutrients are more efficiently absorbed and less are utilised by the gut wall due to a thinner epithelium; second, more nutrients are available to the host because of a reduced flora; third, there is a reduction in harmful gut bacteria which may reduce performance and cause subclinical infection; fourth, production of growth-suppressing toxins or metabolites is reduced; fifth, microbial deconjugation of bile acids is reduced. As the use of AGP was found to be a very cost-efficient way of increasing productivity in pig production, the use of AGP grew steadily during the 1990s in most European countries. For instance, the use of AGP for pigs in Denmark increased from 67 t active compounds in 1989 to 116 t active compounds in 1997 (Anonymous, 1999). The use of antibiotics as AGP clearly exceeded the therapeutic use of antibiotics in animal production and the use of antibiotics in man (Anonymous, 1999).

AGP are poorly absorbed from the lumen of the gut and exert a selective pressure on the commensal microflora. Most AGP are active against Gram-positive bacteria (Jensen, 1998), and although AGP are added to the feed at sub-therapeutic levels (e.g. avorparcin at 20–40 mg/kg, depending on the age-group), the constant selection pressure is sufficient to inhibit the growth of susceptible bacteria and markedly influence the composition of the flora of the gut (Jensen, 1998). For instance, the high selective pressure associated with the use of the glycopeptide avoparcin in animal feed is considered responsible for the occurrence of vancomycin-resistant *Enterococcus faecium* (VRE) in food animals reported in a number of countries (Wegener *et al*. 1999). As *Ent. faecium* is untreatable with practically all other antibiotics, the reports of the first high level of VRE caused great worry among medical practitioners concerned about their ability to treat diseases (Leclerq *et al*. 1988). VRE is frequently present in foods, and direct as well as indirect evidence suggests that the resistance genes can be transmitted from animal to human flora (Wegener *et al*. 1999). Twenty-two pig herds were compared on the basis of occurrence of VRE in faecal samples (Bager *et al*. 1997). A strong and statistically significant ($P < 0{\cdot}05$) association between the presence of VRE and the use of avoparcin was observed. Of twelve herds given avoparcin in feed, eight had VRE, while of ten herds not given avoparcin, two had VRE ($P = 0{\cdot}043$, risk ratio 3·3 and 95 % CI 1·1, 10·0). The association between the use of avoparcin and VRE can also be observed at the national level. In countries where avoparcin had been used as an AGP, VRE could frequently be cultured from food animal faeces whereas in countries where avoparcin had not been used, e.g. Sweden and USA, VRE was not detected (Wegener *et al*. 1999). Results from The Netherlands further showed that VRE was not present in faeces from strict vegetarians, but was present in faeces from human subjects consuming a mixed diet. This finding supports the view that the source of VRE is contaminated meat (Schouten *et al*. 1997).

Following the ban of avoparcin in animal feed, there has been a marked reduction in VRE in animals in Denmark and Germany. In 1995, 82 and 100 % of the poultry flocks in Denmark and Germany respectively had VRE, which declined to 12 and 25 % respectively in the two countries in 1997 (Bager *et al*. 1999). VRE in pigs is also declining but more slowly. In 1995 VRE was identified in approximately 20 % of the herds, which was reduced to <10 % in 1999 (Bager *et al*. 1999). The relatively slow elimination of the resistant bacteria in pig herds has also been observed in the UK. The use of tetracycline for pigs was discontinued in the UK in 1971, because of concerns about the spread of antibiotic-resistant pathogenic bacteria. Despite this ban, there was no significant decrease in the incidence of pigs harbouring tetracycline-resistant *Escherichia coli* in their faeces in 1975 (Smith, 1975). Similarly, Langlois *et al*. (1983) found that the withdrawal of antibiotics from pig feed over 10 years led to a reduction in the incidence of tetracycline-resistant bacteria of only about 50 %. In addition to the obvious influence of AGP on the detection of resistant bacteria, the herd environment, history and cross-contamination are also thought to influence the level of antibiotic resistance of the gut microflora.

The gastrointestinal tract of pigs and its commensal microflora

The various gastrointestinal regions have different structures and functional elements that provide optimal conditions for the digestion and absorption processes of the tract. Gastric emptying regulates the flow of digesta from the stomach to the small intestine (Low, 1990), and the digesta moves at a higher velocity in the proximal small intestine compared with the more distal segments. Dietary inputs and the secretions from the stomach, intestine, pancreas and gall bladder largely determine the composition of the digesta in the stomach and the upper part of the small intestine (Johansen & Bach Knudsen, 1994; Johansen *et al*. 1996). As the digesta moves distally, flow rate and O_2 content decline, and the composition changes as a result of digestive, secretory and microbial processes. The mucosa of the small intestine 'traps' the nutrients released by the hydrolytic processes (glucose from starch, amino acids and peptide from proteins, and fatty acids and glycerol from lipids) and absorbs them into the body (Gray, 1992). The epithelium is a semi-permeable layer that efficiently regulates the exchange of materials between the body and the lumen contents, and is metabolically very active. Furthermore, the secretions and the glycoproteins of the brush-border membrane influence the adherence and the metabolic activity of bacteria (Kelly *et al*. 1994). There are also regional differences in the mucosal architecture, and the height of the villi is reduced from the proximal (e.g. the regions with high nutrient influx) to distal small intestine, with very few villi present in the colon (Jin *et al*. 1994; Brunsgaard, 1997).

The gastrointestinal tract of pigs is densely populated with bacteria. The population of bacteria (viable counts/g

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fresh material) increases from 10^7–10^9 in the stomach to 10^9 in the distal small intestine, and further to 10^{10}–10^{11} in the colon, and with an increasing proximal to distal abundance of obligate anaerobes (Bach Knudsen *et al*. 1993*a*; Jensen & Jørgensen, 1994). The majority of the culturable bacteria in the colon are Gram-positive strictly-anaerobic streptococci, lactobacilli, eubacteria, clostridia and peptostreptococci, while Gram-negative organisms comprise about 10 % of the total culturable flora. In an extensive study of pig faecal bacteria by Moore *et al*. (1987) the most common isolates were *Streptococcus* spp., representing 27·5 % of all isolates. *Lactobacillus, Fusobacterium, Eubacterium, Bacteroides* and *Peptostreptococcus* were the next most common bacteria. The bacterial composition is under the influence of dietary composition, which has a high impact on the population and activity of the commensal microflora. In addition to the horizontal variation in bacterial composition, there is also a vertical gradient of species distribution (Kelly *et al*. 1994). The mucosa provides an environment that differs physically and chemically from those of the digesta. It is also recognised that the bacteria associated with the mucosa are likely to have a greater potential to influence the host than those present in the lumen (Kelly *et al*. 1994). However, much more is known about the bacteria of the lumen than about those attached to the mucosa.

On the basis of the interaction between the microflora and the host, and of their metabolic activity, the different bacteria can be categorised into those that are considered beneficial (lactobacilli and bifidobacteria) and those that have the potential to detrimentally affect the host (coliform; Gibson & Roberfroid, 1995). Although the importance of the resident bacteria for health and disease is well recognised, little is understood of the interaction between the diet, the microflora, the host and the implications for health and disease.

Influence of dietary carbohydrates on the physiology of the gut

Dietary carbohydrates constitute a major proportion of pig diets (Bach Knudsen & Jørgensen, 2001). The carbohydrate fraction consists of mono-, di- and oligosaccharides and two broad classes of polysaccharides (starch and NSP; Theander *et al*. 1989; Bach Knudsen, 1997). The carbohydrate fraction has a diverse composition in terms of constituent sugars (pentoses, hexoses, deoxysugars, etc.), glycosidic linkages (α or β), size (degree of polymerisation from one to several thousand) and physical form (soluble in water, insoluble, cation-binding and adsorbing properties; Theander *et al*. 1989; Bach Knudsen, 2001).

The composition of the carbohydrate fraction influences the digestion and absorption processes of carbohydrates and other nutrients in the various parts of the gastrointestinal tract (Bach Knudsen & Jørgensen, 2001); it has a profound influence on the secretory response of the gut to feed intake (Low, 1989), the volume flow (Bach Knudsen *et al*. 1993*a*), the mucosal architecture (Jin *et al*. 1994; Brunsgaard, 1998), composition of the gut flora (Jensen & Jørgensen, 1994) and the development of the gastrointestinal tract (Jørgensen *et al*. 1996). Digesta materials that are collected from the stomach resemble to a high degree the composition of the diets, while endogenous materials become relatively more important as the digesta materials move distally in the small intestine. In ileal digesta carbohydrates typically account for 30–50 % of the dry residue (Bach Knudsen & Canibe, 2000). In the large intestine dietary carbohydrates are degraded to various degrees, with insoluble lignified fibres (oat hull, wheat bran, etc.) usually resisting degradation to a high degree, while soluble fibres are usually well degraded (sugarbeet fibre etc.; Bach Knudsen & Jørgensen, 2001).

The intestinal mucosa of the pig lacks the enzymes capable of cleaving a number of oligosaccharides that are naturally present in plant materials (i.e. raffino-oligosaccharides, fructo-oligosaccharides) or used as feed additives (i.e. neosugar, *trans*-galacto-oligosaccharides). Collectively these oligosaccharides are referred to as non-digestible oligosaccharides (NDO; Van Loo *et al*. 1999). NDO were previously considered as an antinutritional factor which could potentially accumulate in the small intestine, cause osmotic diarrhoea and, because of their rapid fermentation and high gas production, cause discomfort for the animals. Recently, there has been a growing interest in NDO because of their possible prebiotic properties, i.e. stimulation of the growth and/or activity of one or a limited number of desirable bacteria in the colon and, thus, exclusion of pathogens (Gibson & Roberfroid, 1995; Van Loo *et al*. 1999). In man it has been demonstrated that inulin and oligofructose, independent of chain length, have significant prebiotic properties by selectively stimulating the growth of bifidobacteria in the colon. Based on observations with more than 100 volunteers differing in sex, age, race and dietary habits, there is strong evidence in human subjects that β(2→1)-type fructans are prebiotic (Van Loo *et al*. 1999). The results from studies with pigs are less convincing (Houdijk, 1998). In a study by Buddington (1998) it was found that the influence of oligofructose on the bacterial population was more pronounced in the small intestine and proximal colon of suckling pigs compared with faecal samples. The reason for this effect is presumably that the NDO, at the low dose used, are metabolised by the flora colonising the stomach and small intestine (Houdijk, 1998). A synergic effect of fructo-oligosaccharide and *Lactobacillus paracasei* was recently observed in an experiment with weaning piglets (Nemcová *et al*. 1999). The total number of anaerobes, aerobes, lactobacilli and bifidobacteria increased while that of clostridia, *Enterobacteriaceae* and *Esch. coli* decreased.

Starch is the most abundant carbohydrate in diets of pigs. Starch is a mixture of the linear α(1–4)-linked amylose and the branched α(1–4),(1–6)-linked amylopectin. Most of the ingested starch is efficiently broken down by the combination of secreted α-amylase and enzymes located on the intestinal surface membrane (Bach Knudsen & Jørgensen, 2001). A variable proportion of starch (resistant starch; RS), however, will be resistant to degradation in the small intestine and may have properties similar to those of NSP. A high-amylose maize-starch diet fed together with *Bifidobacterium longum* increased the number of bifidobacteria in the faeces compared with a low-amylose maize-starch diet (Brown *et al*. 1997). The mechanism whereby high-amylose maize starch raises the faecal probiotic numbers is uncertain, but a number of possibilities have been discussed. First, the RS in high-amylose maize starch may have a

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diluting effect in the upper part of the gastrointestinal system, thus protecting the bacteria against bile acids, free fatty acids, partial acylglycerols and other products of digestion that have bactericidal actions. Second, the bacteria may have been protected by adhesion to undigested starch or through pits formed in the starch granules during intestinal amylosis. A final possible mechanism could be that the high-amylose starch simply acts as a substrate for the bifidobacteria. To obtain any specific effects of starch on the gut flora, starch has to be fed together with a probiotic, as there is little evidence that the starch would have any specific stimulatory effects on beneficial micro-organisms (Sgorbati *et al*. 1995).

NSP are the main carbohydrate fraction not digested by enzymes in the pig small intestine (Bach Knudsen, 2001). However, because of the microbial colonisation of the stomach and small intestine, some disappearance of NSP occurs in the upper intestinal tract. This degradation is caused by the microflora colonising these sites of the gastrointestinal tract. Based on results reported from fifty-one digestibility trials using ileally-cannulated pigs, the average digestibility of NSP as far as the end of the small intestine was found to be 24 %, with large variations between experiments (range −10 to +62 %; Bach Knudsen & Jørgensen, 2001). The results obtained with cereal diets consistently show a higher digestibility of the linear and relatively-soluble mixed-linked β(1–3), (1–4)-D-glucan (β-glucan) compared with the branched-chain arabinoxylans from wheat, rye and oats. β(1–3), (1–4)-D-glucan-rich diets, i.e. barley and oats, also seem to stimulate the formation of lactic acids in the small intestine (Bach Knudsen & Canibe, 2000), presumably because of prebiotic properties of β(1–3), (1–4)-D-glucan. In a study by Graham *et al*. (1986) it was found that lactic acid-producing micro-organisms (lactobacilli) were responsible for the significant degradation of β(1–3), (1–4)-D-glucan in the upper intestine of pigs.

The main site for NSP degradation is the large intestine (Bach Knudsen & Jørgensen, 2001). At this site, digesta are retained for prolonged periods of time (generally 20–40 h), which allows prolific bacterial growth. Several studies have shown that NSP is the carbohydrate source entering the large intestine in quantitatively the largest amount (Bach Knudsen & Jørgensen, 2001). It has also been shown that NSP have a strong influence on the activity and composition of the commensal microflora. However, NSP do not seem to have a selective influence on specific strains of micro-organisms, as has been established for some NDO (i.e. various fructans), and very little is known about how the different groups of resident micro-organisms interact with pathogenic species of bacteria.

The outcome of fermentation of carbohydrates present as NDO, RS or NSP is production of short-chain fatty acids (SCFA), mainly acetate, propionate and butyrate, and the gases H_2, CO_2, and CH_4. The production of SCFA and gases is under the direct influence of dietary carbohydrate composition, since production increased in response to more carbohydrates entering the large intestine (Bach Knudsen *et al*. 1993*a*; Jensen & Jørgensen, 1994). Rapid generation of SCFA lowers the pH; a horizontal gradient is usually seen along the large intestine, with the pH in caecum being significantly lower ($P < 0{\cdot}001$) than that in distal colon (Bach Knudsen *et al*. 1991). The SCFA produced are rapidly absorbed from the gut lumen, and the absorption rate is driven by the concentration gradient between the lumen and the portal vein. The concentration of SCFA in the gut lumen is for most types of diets in the range 100–140 mmol/kg digesta, but some special types of diets, e.g. diets based on sugarbeet fibre, may raise the level in the lumen to 150 mmol/kg digesta (Petkevicius *et al*. 2001). The reason for this increase is at present unknown, but may be related to the type of residual carbohydrates accumulating during passage through the colon.

In vitro and *in vivo* studies show that the molar ratios between the main SCFA may be influenced by dietary carbohydrate composition, as some types of plant materials not only increase the production of total SCFA, but also influence the ratios between the individual acids (Bach Knudsen *et al*. 1993*b*; van den Meulen *et al*. 1997; Christensen *et al*. 1999). The SCFA produced are metabolised in different tissues; most of the butyrate being cleared in the large intestinal epithelia, propionate is converted to glucose in the liver, whereas acetate is used in muscle tissue (Bergman, 1990). There is good evidence that the SCFA produced influence epithelial cell proliferation, intestinal tissue mass, the absorption of water and solutes, and mucus secretion (Sakata, 1997). All these factors are of importance in maintaining the function and health of the large intestine.

The role of carbohydrates in the control of enteric bacterial infections of pigs

As discussed earlier, dietary carbohydrates play an important role in the function of the gastrointestinal tract of pigs. Research carried out in Australia seems to suggest that the diet may help to control enteric bacterial infections. Swine dysentery is a major problem in many parts of the world. The disease is caused by the anaerobic intestinal spirochaete *Brachyspira (Serpulina) hyodysenteriae*, which colonises the crypts of the large intestine and induces severe mucohaemorrhagic colitis and dysentery (Hampson *et al*. 1997). Studies with gnotobiotic pigs have shown that colonisation by the spirochaete and lesion formation is enhanced by the presence of other species of anaerobic bacteria (Whipp *et al*. 1979). Earlier field studies have indicated that there is a protective effect when pigs with swine dysentery are changed from a maize-based diet to a diet based on maize silage (Prohaszka & Lukacs, 1984). The interpretation was that the maize silage lowered the pH of the digesta in the large intestine, thereby inhibiting the growth of *Brach. hyodysenteriae*. A series of studies performed by one Australian group (Hampson and his co-workers), however, did not confirm this interpretation. Rather, the Australian studies indicated that a very digestible diet based on cooked white rice and animal protein is protective against colonisation by the spirochaete, or against development of swine dysentery after experimental challenge (Pluske *et al*. 1996; Siba *et al*. 1996). When the cooked rice or the animal protein was mixed with either lupin (*Lupinus* spp.) or wheat, disease occurred after challenge. The authors identified the protective effect to be the low level of NSP and RS in cooked rice that limited fermentation in the large intestine, and in this way suppressed the commensal microflora which

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normally facilitate colonisation by the spirochaete (Pluske *et al*. 1998). A direct physical effect of the limited amount of residue that is passed to the large intestine could also play a role. In a follow-up study maize and sorghum, when steam-flaked, also reduced the incidence of disease after experimental challenge, and soluble NSP and RS were identified as two important dietary components that promote fermentation in the large intestine and were associated with high incidence of swine dysentery (Durmic *et al*. 1997, 1998). This hypothesis was further investigated in a follow-up study in which either soluble NSP in the form of guar gum or RS as retrograded maize starch was added to the protective cooked-white-rice plus animal-protein diet (Pluske *et al*. 1998). Pigs fed the diets supplemented with either soluble NSP or RS became colonised and developed swine dysentery, while those on the control diet did not. In line with the hypothesised protective role of the limited fermentation in the large intestine, a diet with added insoluble NSP from oat chaff showed a protective effect, similar to that obtained with the rice diet (Pluske *et al*. 1998). The potential of using exogenous enzymes to improve the digestibility of wheat- and sorghum-based diets, and thereby to obtain a similar protective effect to that of the cooked-white-rice diet, has also been tested with variable results (Durmic *et al*. 1997).

The Australian research has consistently shown the cooked-white-rice diet supplemented with animal protein to have a protective effect against the expression of swine dysentery after experimental challenge. However, it has been difficult to reproduce these findings outside Australia. In a Danish study in which the pigs were fed a standard diet based on wheat, barley, soyabean meal and fish meal, cooked white rice plus animal protein, or the rice diet supplemented with raw potato starch, wheat bran or sugarbeet pulp, or a fermented liquid standard diet or a standard diet supplemented with 2 % (v/w) lactic acid, the rice diet did not prevent the development of swine dysentery on experimental infection (Lindecrona *et al*. 2000). Increasing the level of NSP or RS did not result in a higher incidence of disease. However, clinical symptoms and pathological lesions were more severe when the level of NSP was increased. In the group that was fed the fermented liquid standard diet the incidence and the severity of clinical signs were lower compared with the other feeding groups, presumably reflecting an impaired colonisation of *Brach. hyodysenteriae* in the large intestine as a result of changes in the microflora (Leser *et al*. 2000) and/or biochemical environment. The reason for the failure in obtaining protection with the cooked-white-rice diet in Denmark compared with Australia is not easy to explain, but could be due to differences in the way the rice is processed, and/or site differences in the commensal flora. Since colonisation with *Brach. hyodysenteriae* requires a component of the anaerobic microflora to be expressed, it may be possible that differences in the intestinal microflora at the study site can influence the outcome.

The strategy of using a highly-digestible rice-based diet to limit colonisation with pathogens has also been explored for *Brachyspira (Sperpulina) pilosicoli*. *Brach. pilosicoli*, like *Brach. hyodysenteriae*, colonise the caecum and colon, but unlike *Brach. hyodysenteriae, Brach. pilosicoli* mainly remain in the lumen and/or the epithelial layer adjacent to the intestinal lumen (Hampson *et al*. 1999). In a study where two groups of weaned pigs were fed either a standard commercial wheat–lupin diet, or a rice-based diet, all the pigs became colonised with *Brach. pilosicoli* (strain 95/1000; Hampson *et al*. 1999). However, the pigs on the rice-based diet became colonised later and the colonisation lasted for a shorter time compared with the wheat–lupin diet, indicating retardation but not full protection by the highly-digestible rice-based diet.

It is well established that post-weaning diarrhoea caused by enterotoxigenic strains of *Esch. coli*, which colonise the small intestine, is a multifactorial condition that is influenced by diet (Hampson, 1997). A high level of dietary protein predisposes to the condition (Prohaszka & Baron, 1980), while various types of dietary fibre have been thought to reduce the incidence and severity of post-weaning diarrhoea (Bertschinger *et al*. 1978). In a study reported by Larsen (1981) oral administration of pectin to pigs reduced the fluid accumulation in intestinal loops challenged by different dilutions of enteropathogenic *Esch. coli* strains. It was concluded that pectin interacts with the bacterial colonisation and that the protective effect was most pronounced with low inoculation doses in the loops (dose 10^3–10^5 enteropathogenic *Esch. coli*), while high doses permitted the strains to exert their enteropathogenic effect. In recent studies, the gastrointestinal-stabilising properties of various pectins differing in dose, degree of methylation (and molecular weight), Ca sensitivity and source were studied under experimental (Lærke *et al*. 2001) and practical conditions. In spite of huge differences in the functional properties of the different pectins (Lærke *et al*. 2001), we were not able to identify any specific beneficial effects of the pectins on the profile of organic acids in the large intestine, or bacterial composition, or the overall health of the animals (HN Lærke, BB Jensen, ALF Hellwing and KE Bach Knudsen, unpublished results). The highly-methylated pectin produced a negative effect on the digestibility at the end of the small intestine and on animal performance (HN Lærke, BB Jensen, ALF Hellwing and KE Bach Knudsen, unpublished results). The latter effect, however, could be due to the pectin being added to a diet already high in dietary fibre.

McDonald *et al*. (1997, 1999) have studied the effect of a highly-digestible diet based on cooked white rice supplemented with animal protein, and a diet with added soluble fibre provided as guar gum. When the pigs on the two diets were challenged with enterotoxigenic *Esch. coli*, significantly more ($P < 0{\cdot}05$) of these organisms were recovered from pigs that were fed the rice diet supplemented with guar gum. The results of this experiment thus suggest that the guar gum had a detrimental effect on the proliferation of enterotoxigenic *Esch. coli* in the small intestine.

Carbohydrates and the control of parasite infections in pigs

Like enteric bacterial infections in pigs, parasites can have a major economic impact on pig production through reductions in daily live-weight gain and feed conversion. As a result of a chance finding (Petkevicius *et al*. 1995), we

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discovered that the dietary carbohydrate composition had a profound influence on the establishment, gut location and fecundity of *Oesophagostumum dentatum* in the large intestine of growing pigs. In a series of studies in which pigs were experimentally infected with *O. dentatum* and fed on diets that provided different types and levels of dietary carbohydrates to the large intestine, it was clearly demonstrated that diets with a high content of resistant fibres (oat-hull meal or wheat bran) provided favourable conditions for the establishment of *O. dentatum* and female worm fecundity, while the opposite was the case when the experimental diet contained fermentable carbohydrates in the form of inulin and sugarbeet fibre (Petkevicius *et al*. 1997, 1999, 2001). More recently, it was also reported that feeding the two contrasting diets could be used to reduce egg excretion and worm numbers (the diet containing fermentable carbohydrates) or to increase egg excretion and worm number (the diet containing the resistant carbohydrates; Petkevicius *et al*. 2001) in pigs with already established infection. The mechanisms behind the protective effect of the diets containing high levels of fermentable carbohydrates have not yet been established, but the effect appears to be related to the increased production of SCFA, which have direct and indirect effects on the large intestine by influencing epithelial cell proliferation, intestinal tissue mass and mucus secretion (S Petkevicius, KE Bach Knudsen, P Nansen and KD Murrell, unpublished results). Thus, dietary carbohydrate composition appears to have a significant influence in controlling *O. dentatum* infection, not only in indoor pigs (Petkevicius *et al*. 1995, 1997, 1999, 2001), but also in pigs on pasture (Petkevicius *et al*. 1996). These findings are in agreement with an epidemiological investigation that points to NSP as the most important factor controlling parasite infection, particularly *Trichuris suis*, in growing pigs in the UK (Pearce, 1999). Moreover, the study of Pearce (1999) further indicated that infection with *T. suis* in many cases was followed by a high incidence of *Lawsonia intracellularis* infection, which points to a synergism between the nematode and pathogenic micro-organism. Such a synergism between the microbial flora and *T. suis* has been identified previously when comparing the clinical syndrome in conventionally-reared pigs, specific pathogen-free pigs and gnotobiotic pigs (Rutter & Beer, 1975). The disease in conventionally-reared pigs was characterised by a severe mucohaemorrhagic enteritis; in contrast, a mild catarrhal enteritis was observed in specific pathogen-free and gnotobiotic pigs. The authors conclude that a microbial component acts synergistically with *T. suis* infection to produce the severe clinical syndrome in conventionally-reared pigs. It was further suggested that the mechanism could be that the emerging *T. suis* larvae stimulate the production of excessive mucus in which the microbial component of conventional pigs multiplies.

Feed structure and the control of *Salmonella* prevalence in pigs

Several epidemiological investigations and reports from advisory bodies pointed to meal feeding rather than feeding with pelleted feeds in order to reduce the risk of subclinical infections with *Salmonella enterica* (Dahl, 1997; Stege *et al*. 2000) and *L. intracellularis* and *Brach. pilosicoli* (Stege *et al*. 2000). Results obtained under practical conditions have shown that the prevalence of *Salmonella* is reduced when coarsely-ground feeds rather than finely-ground pelleted feeds are fed (Jørgensen *et al*. 1999). The feed structure is related to the carbohydrate composition, in particular the fibre content of the raw material; for example, barley produces a more coarse meal than wheat when milled to pass the same screen size (Nielsen, 1998). In the digestive tract coarsely-ground feed and feed with a higher dietary fibre content give rise to digesta material that is more coherent, with little separation between the solid and liquid phases of digesta (CF Hansen, L Jørgensen and KE Bach Knudsen, unpublished results), which in turn results in a higher DM content and a lower pH in the gastric contents at slaughter compared with finely-ground pelleted feed (Jørgensen *et al*. 1999). It is likely that the greater proportion of solid digesta produced after feeding the coarsely-ground feed influences the microbial ecosystem in a way that provides *Salmonella* with poorer growing conditions compared with pelleted feeds. These results further confirm that coarsely-ground materials have a positive influence on gastric health, which may be an ethical rather than a production problem for the pig industry (Simonsson & Björklund, 1978; Nielsen, 1998). The feed structure and dietary fibre composition also influence the morphology of the gastrointestinal tract, its architecture, and the production and composition of mucus; which may possibly play a role in combating enteric infections (Brunsgaard, 1998).

The downside of the use of feed structure to control *Salmonella* infection, however, is the negative impact it has on performance (Jørgensen *et al*. 1999). As a result of the coherent properties of coarsely-ground materials, there will be a bigger risk of encapsulation of otherwise available nutrients, which are then not available for digestion by enzymes in the small intestine. In many cases there has been a significant increase ($P < 0{\cdot}001$) in the faecal excretion of starch (Jørgensen *et al*. 1999). A factor that may also contribute to the negative influence of coarse feed on animal performance is stimulation of gastric and pancreatic secretions, which has also been reported when increasing the fibre level (Low, 1989), and which from an energetic point of view is costly. Thus, more work needs to be done to improve production economy without any adverse effects on gastric health and *Salmonella* prevalence.

Other means of influencing gut health

There are a number of other possible means of influencing gut health that are not covered in the present paper. The most important of these are organic acids that are used to inhibit or kill pathogenic bacteria, controlled-fermented liquid feeds, inorganic chemicals (e.g. ZnO), bacteriophages or bacteriocins, strategies for improving the local immune responses, and long-term approaches such as selective breeding of animals for resistance to infectious diseases.

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Conclusion

As there is a risk of developing antibiotic resistance, a number of commonly-used AGP have been banned in the EU member states. This decision has put new emphasis on using the diet to control enteric bacterial infections in pigs. Dietary carbohydrates constitute a major proportion of diets for pigs, and the carbohydrate fraction has a diverse composition, with different properties in the gastrointestinal tract, some of which are of importance to gut health. Findings from different studies indicate that dietary carbohydrate composition influences the expression of swine dysentery and infection with nematode worms after experimental challenge with *Brach. hyodysenteriae* and *O. dentatum* respectively. There is also increasing evidence that the feed structure can be used to reduce *Salmonella* prevalence at the herd level. However, it should be stressed that using the diet to manage gut health is not straightforward, since the expression of a pathogen in many cases requires the presence of other components of the commensal biota.

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