Physiology of Small and Large Intestine of Swine*
- Review -

R. Mosenthin[1]

Hohenheim University, Institute of Animal Nutrition, D-70593 Stuttgart, Germany

ABSTRACT : The small and the large intestine of swine represent the organs that extract nutrients from feedstuffs through digestion and fermentation and that allow their absorption and incorporation into the blood circulation. Special attention is directed towards the small intestine of young pigs since the transition to a solid diet at weaning exerts major impacts on the structural and functional integrity of the small intestine. Dietary factors involved in postweaning changes of gut morphology and biochemistry such as removal of bioactive compounds in sows milk at weaning, anti-nutritional factors in weaner diets, dietary fiber and the role of voluntary feed intake will be elucidated. The microbial function of the large intestine which is carried out by a diverse population of microorganisms is dependent on substrate availability. Short chain fatty acids as main fermentation products contribute to the energy supply of the host but they are also important for the maintenance of the morphological and functional integrity of the epithelium in the colon. As a result of bacterial nitrogen assimilation in the large intestine, nitrogen is shifted from the urinary to the fecal excretion route thus saving metabolic energy to the pig because less ammonia would become available for conversion to urea.

(**Key Words**: Small Intestine, Large Intestine, Physiology, Swine)

INTRODUCTION

The gastrointestinal tract (GIT) of animals acts as the barrier between the outside world and the extracellular fluid of the body. It is responsible for the digestion and absorption of nutrients and energy, but it also excludes pathogenic compounds such as bacteria and toxins from entering the body. The central role of the GIT in the whole organism nutrient requirements is a function of the gut mass, which reflects the number and metabolic activity of its constituent cells. Since these cells possess complex morphological specializations, the GIT is a highly differentiated structure. In monogastric animals the gut can be physiologically categorised into the stomach, small intestine and large intestine. These different segments of the GIT have in common their ability to digest feedstuffs before absorption. However, as has already been stated by Pekas (1991), digestion and absorption are integrated functions, i.e. digestion can not be separated from absorption. Hydrolysis by host enzymes plays an important part, especially in the small intestine. But its functions are not confined to chemical reactions since digestion also occurs through fermentation which takes place predominantly in the large intestine. Absorption of nutrients from the lumen of the GIT begins with their transport, active or passive, across the membrane of the epithelial cells lining the mucosal surface. This is followed by passage across the cells, and entry into the blood or lymphatic system.

The main objective of this review is to describe the physiology and biochemistry of the small and large intestine and review factors affecting its structure and function. Special attention will be given to the small intestine, firstly because the small intestine is the principal digestive-absorptive organ and secondly, because swine experience a major shift in the composition and quantities of the dietary loads when they are weaned from sow milk to a solid diet resulting in functional demands on the intestine.

Small intestine physiology

The small intestine which includes the duodenum, jejunum and ileum can be up to 20 m in length and can

[1] Address reprint requests to Prof. R. Mosenthin.

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account for one third of the total volume capacity of the whole GIT (Moran, 1982). Digestion and absorption in the small intestine is made more efficient by a significant increase in its epithelial surface area which is provided by the mucosa, with the *villi* and *microvilli* increasing the surface area ten-fold and thirty- to sixty-fold, respectively (Caspary, 1987, Smith, 1992). In addition, the surface area of the small intestine is increased by numerous spiral or circular folds of the *submucosa* of the gut by a factor of three (Caspary, 1987). According to Buddle and Bolton (1992), the small intestine of a 3kg-piglet of 10 days of age has a total absorptive area of 114 m^2. However, the digestive-absorptive capacity of the small intestine is not fixed at each stage of development; it adapts and responds to different dietary factors and it is dependent on a wide variety of factors that may affect the rate and extent of nutrient digestion and absorption as summarized in table 1.

Table 1. Summary of factors affecting digestion and absorption in the small intestine of pigs

Mode of ingestion
Digestibility
Gastric emptying
Intraluminal digestive capacity of the pancreas and bileTransit time (contact time for digestion and absorption)
Contact surface
– Length of intestine
– Surface of villi and microvilli
– Enzyme content of brush border membrane
– Carrier function
– Theickness of the diffusion barrier of the absorptive epithelium

Adapted from Caspary (1992).

The contact surface of the small intestine is represented by the mucosal surface which, in turn, consists of three layers with the *muscularis mucosa* as the deepest layer that separates the mucosa from the submucosa. The middle mucosal layer, the *lamina propria* is attached above by the epithelium and below by the *muscularis mucosa*; together with the epithelium it provides structural support and the vascular, lymphatic and neural elements for the epithelium. However, it is the third layer of the intestinal mucosa that is in direct contact with the contents in the lumen. A single sheet of columnar cells, the enterocytes, line the villi and surrounding crypts. The villi are outgrowths (300 to 500 μm in length) of the mucous membrane whereas the area available for digestion and absorption is increased further by microvilli (~1 μm in length), which are extensions of the epithelial membrane. The microvilli are coated by a glycoprotein, the *glycocalyx*; the combination of both is known as the "brush border membrane". It contains a wide variety of enzymes responsible for the final digestion of carbohydrates and proteins. In addition, special carrier proteins which are necessary for the absorption of different types of nutrients such as sugars, amino acids and minerals, are located on the surface of the microvilli. *Goblet* cells that are scattered amongst the enterocytes provide mucus that form a protective and lubricating layer on the epithelium. Between the bases of the villi are the crypts of *Lieberkühn*, tube-like structures, that penetrate the thickness of the mucosa membrane almost to reach the *muscularis mucosa*.

The level of feed intake appears to be a critical messenger in the regulation of the digestive-absorptive capacity in the small intestine. When pigs were fed according to three different feed restriction schedules, the responses were specific to the mucosa (Pekas, 1991). As it can be derived from table 2, mucosa accounted for 108. 3% of the weight change of the small intestine, followed by musculature (49.5%) and the remainder of tissue (12.4 %). In addition, studies by Kelly et al. (1991c) showed that these mucosal responses were associated with corresponding responses of the villi and thus of the epithelial surface area. Adaptive responses of digestive-absorptive capacity in the small intestine as influenced by differences in composition and quality of protein, fat, starch and fiber, were reviewed by Pekas (1991) and will not be reported in this review.

Table 2. Effect of different feeding schedules on the weight (g) of tissue components of the small intestine of pigs

	Treatment[1]			Response
	HL	MM	LH	HL vs LH, HL = 100
Total tissue	640	869	1,182	+85
Matrix	89	94	100	+12
Muscle	112	129	167	+49
Mucosa	439	646	915	+108

[1] HL: high-low; MM: medium-medium; LH: low-high (All refer to the plane of nutrition in two sequential periods)

Adapted from Pekas (1991).

Postweaning changes in the structure and function of the small intestine

Weaning can be a critical period for swine. The transition to a solid diet can be abrupt in production

settings and is usually accompanied by a lower feed intake, an increase in malabsorption and disease and lower growth rate as was reviewed by Buddington (1997). Under normal circumstances (before weaning) the constant cell turnover in the intestinal epithelium is maintained by a dynamic equilibrium between cell production at the base of the crypt and cell loss at the top of the villus (Clarke, 1973). It should be mentioned that the rate of cell turnover in the epithelium of the small intestine is the fastest of any tissue in the pig (Pekas and Wray, 1991), i.e. two to four days are needed to replace the entire villous epithelium of a three week old piglet (Moon, 1971).

Histological and morphological measurements of the GIT of piglets, in particular when combined with the measurement of functional activities (e.g. enzyme production), have revealed that important changes occur with age and at weaning. Various reports have shown that histological changes are induced in the mucosa of the small intestine of piglets after weaning (Kenworthy, 1976; Smith, 1984; Hampson 1986 a, b; Miller et al., 1986; Cera et al., 1988; Kelly et al., 1990b; 1991b; 1991c, Li et al., 1990; Nabuurs et al., 1993; Pluske et al., 1996b; 1996c). These reports show a reduction in villous height (villous atrophy) and an increase in crypt depth (crypt hyperplasia) after weaning. If villous atrophy occurs via an increased rate of cell loss, then this is associated with increased crypt cell production and hence increased crypt depth; however, villous atrophy may also result from a decrease in the rate of cell renewal which is the result of a reduction in cell division in the crypts. These morphological changes which can be modified by the type of microflora present in the small intestine and dietary factors (refer to next section of this review) are more conspicuous when weaning occurs at an earlier age. Weaning at two weeks of age decreases villi length and increases crypt depth; weaning at three weeks of age increases crypt depth (Smith, 1984). At the same time, alanine transport in *in vitro* studies is higher in three week- compared to two week-old piglets and is confined to enterocytes in the area of the villus tip. According to Hampson (1986a), villous height was reduced to 75% of pre-weaning values within 24 hours after weaning and continued to decline until the fifth day after weaning to approximately 50% of the initial values found at weaning. These findings were confirmed by Miller et al. (1986) whereas Cera et al. (1988) reported a reduction in the length of microvilli for three to seven days after weaning. Pigs that were not weaned, however, showed only small reductions in villous height. As a result of these changes in villous height and crypt depth after weaning, the villous to crypt ratio in weaned piglets is significantly reduced compared to pigs that are not weaned.

These morphological responses to weaning have a great effect on mucosal functions in the small intestine. Several reports clearly show that villous atrophy and crypt hyperplasia is usually associated with a decline in the activities of the brush border enzymes (Hampson and Kidder, 1986; Miller et al., 1986; Kelly et al., 1991b; 1991c). According to Miller et al. (1986) structural (morphological) changes in the small intestine after weaning are associated more with enzymatic than with absorptive functions. The age-dependent decrease in lactase activity in unweaned piglets (Miller et al., 1986, Kelly et al., 1991a) is suppressed by weaning and this suppression is more severe than that of α-glucosidase (Miller et al., 1986). The specific activities of lactase and sucrase reached minimum values at four to five days after weaning, irrespective if creep feed was offered prior to weaning or not (Hampson & Kidder, 1986). Activities of maltase-2 and maltase-3 showed no change in pigs up to four weeks of age, but increased in response to weaning at six weeks of age (Miller et al., 1986). Similarly, the transition to a solid diet at two weeks of age resulted in increased activities of maltase and α-amylase which can be attributed to rapid substrate induction of these carbohydrases (McCracken, 1984; Kelly et al., 1990b; 1991c).

Digestive enzyme activities in the stomach and pancreas have also been examined in response to weaning. Proteolytic activity in gastric and intestinal digesta increases sharply within six days after weaning (Efird et al., 1982b). In agreement with these results recent studies by Rantzer et al. (1997a) showed a significant increase in the volume of pancreatic secretions as well as the secretions of protein and trypsin during the first five days after weaning. Gestin et al. (1997) as well as Rantzer et al. (1997b) concluded that the mechanisms for the modulation of the development of the pancreas at weaning probably involve several factors including the stage of development, level of feed intake and feed composition. According to Gestin et al. (1997), elastase-2 and chymotrypsin are the predominant pancreatic proteases during the neonatal period whereas elastase-1, trypsin and also α-amylase are probably more specifically expressed after weaning.

Although several reports indicate that villous atrophy and crypt hyperplasia and loss of digestive enzyme activity after weaning may reduce the digestive and absorptive capacity for nutrients such as D-xylose (Hampson & Smith, 1986), alanine (Miller et al., 1986), glucose and electrolytes (Nabuurs et al., 1994), these

findings are questioned by other authors. For example, Kelly et al. (1990b) and Pluske et al. (1996c) did not find a reduction in the ability of villi to absorb D-xylose after weaning. The reasons for the discrepancies are not clear but it can be derived from studies by Kelly et al. (1991c) and Pluske et al. (1996a) that measurements of digestive enzyme activities *in vitro* (such as specific lactase and sucrase activities) can only provide an approximate assessment of digestive capacity and these should be verified by *in vivo* studies of digestion and absorption. It appears that an increase in intestinal growth, and hence total surface area, of the small intestine after weaning compensates for a decrease in the efficiency of absorption. Puchal and Buddington (1992) demonstrated that sugar and amino acid uptakes per unit of weight of intestine at weaning were significantly lower than those measured at birth; however, because of intestinal growth (Efird et al., 1982a) absorptive capacities of the entire small intestine increased and remained matched to higher dietary loads of nutrients. This information can not be obtained using current *in vitro* methods of assessment.

Dietary effects on the physiology of the small intestine after weaning

Dietary and nutritional factors contribute to a large extent to changes that occur in the structure and function of the small intestine after weaning. These include (a) removal of bioactive compounds in sows milk at weaning, (b) anti-nutritional factors in weaner diets, (c) dietary fiber, and (d) the level of feed intake after weaning. Although these factors are described separately, it should be mentioned that they act either independent or interact with other factors. However, possible interactions with the epithelium of the small intestine in response to the proliferation of enteropathogenic bacteria such as *Escherichia Coli* will not be discussed in this section. Nutritional influences on the interactions between enteropathogenic bacteria in the small intestine and the intestinal mucosa were recently reviewed by Hampson (1994), Kelly (1994) and Kelly et al. (1994a).

Removal of bioactive compounds in sows' milk at weaning

Colostrum and milk contain a large number of bioactive peptides such as growth factors, hormones or cytokines which occur naturally or are derived following proteolysis of milk proteins. Most of these peptides remain biologically active following intestinal transit and translocation into the circulation. Their biological effects are mediated through activation of specific receptors and include regulation of cell growth, differentiation and metabolism of intestinal and peripheral tissues. Since sows milk as a natural source of these compounds is removed abruptly at weaning, this will leave the small intestinal epithelium devoid of these substances and significant effects on postweaning differentiation and development of the small intestine can be expected. In addition, polyamines as well as L-glutamine are found in high concentrations in porcine milk and intestinal tissue (Kelly et al., 1991d; Wu and Knabe, 1994) which suggest that their removal from the diet at weaning may also affect gastrointestinal functions.

The presence of large amounts of epidermal growth factor (EGF) in sows' milk, combined with the low production by the neonate indicates that milk is a major source of EGF for suckling pigs (Tan et al., 1990). The permanent presence of EGF receptors in the intestinal epithelium during growth of piglets supports the idea of EGF as a modulator in the functional development of the gastrointestinal tract (Menard and Pothier 1991, Kelly et al., 1992). Despite the fact that exogenous EGF administration might induce intestinal growth and microvilli enzyme activities (Jaeger et al., 1990), studies by James et al. (1987) reveal that these effects on intestinal structure and function are of a small magnitude.

Insulin and insulin-like growth factors (IGF) are present in physiologically significant concentrations in colostrum and milk (Simmen et al., 1988). The gut appears to be one of the most sensitive target sites since specific IGF receptors are located in the intestine (Morgan et al., 1995). It is generally agreed that IGF's appear to function in a differentiation capacity in the neonatal intestine and regulate the development of brush border proteins (Kelly et al., 1994b, Morgan et al., 1995). Modest growth responses have been reported following oral administration of IGF to colostrum-deprived piglets (Morgan et al., 1995). Burrin et al. (1995) found an increase in intestinal weight and height of villi in the jejunum of piglets by 28 and 78%, respectively, when pigs deprived of colostrum received a milk replacer fortified with IGF-1 for four days. Similar results were obtained by Dunshea and Walton (1995) who reported both an increased growth rate of the piglets and an increased growth rate of the small intestine, spleen and pancreas following infusion of an IGF-1 analogue during suckling. Since the content of growth factors in sows' milk declines with advancing lactation, the aforementioned authors point out that the dietary supply of the newly-weaned pig with exogenous growth factors such as IGF-1 and/or its analogues might be an opportunity to stimulate gut growth and development. This might be of particular importance for the early-weaned pig since its

gut is relatively immature and often challenged by enteropathogenic bacteria.

Virtually all food and feeds contain polyamines; spermidine and spermine are the most abundant polyamines in sows' milk (Kelly et al., 1991d; Motyl et al., 1995). Furthermore, biosynthesis of polyamines occurs in the enterocytes with L-arginine as the main precursor. In the enterocytes of the weaned pigs spermine is the most abundant polyamine, followed by spermidine and putrescine (Blachier et al., 1992). During the neonatal period polyamines play an important role in the intestinal maturation (Dufour et al., 1988); after weaning polyamines are involved in the turnover of the intestinal mucosa by interfering with synthesis of cellular macromolecules (i.e. DNA, RNA). Bardocz (1993) points out that a continuous supply of polyamines is essential for the renewal and functioning of the entire digestive tract since the gut epithelium has the highest cell turnover rates. As there is growing evidence that luminal polyamines directly stimulate mucosal growth (Blachier, 1997) their absence from the diet at weaning may be responsible for negative changes in gut structure and function after weaning. Kelly (1994) showed that hormones, growth factors and other nutrients that stimulate intestinal differentiation also increase intracellular concentration of polyamines. As can be derived from studies by Olanrewaja et al. (1992) the trophic action of IGF-1 is dependent on the biosynthesis and exogenous supply of polyamines.

Data by Wu and Knabe (1993) suggest that L-glutamine may play an important role as energy substrate for the enterocytes of weaned piglets. These authors measured a significant increase in the oxidation rate of glutamine to CO_2 in the enterocytes of piglets weaned at 29 days of age compared to 21-day-old suckling piglets. Furthermore, a recent study by Kandil et al. (1995) showed that glutamine stimulates the activity of ornithine decarboxylase and proliferation at a porcine jejunal enterocyte line. It should be mentioned here that ornithine decarboxylase is responsible for the decarboxylation of ornithine leading to the production of putrescine, one of the polyamines that may stimulate mucosal growth (see previous section). Considering that L-glutamine is the most abundant amino acid at day 22 and 29 of lactation (Wu and Knabe, 1994), the removal of sow milk at weaning may induce villous atrophy which can not be compensated by the endogenous supply of glutamine from muscle and plasma to the intestinal epithelium to maintain villous integrity. There is growing evidence in the literature that glutamine may be considered a conditionally-essential amino acid for the weaned piglet. For example, supplementation of weaner diets with free glutamine prevented villous atrophy (Meier et al., 1993). In addition, DNA concentration and mucosal protein content, as indicators of intestinal integrity, were increased following the consumption of free glutamine (Ayonrinde et al., 1995). There is even some evidence that luminal glutamine may have a beneficial effect on mucosal permeability under conditions of enteric infection (Dugan and Mc Burney, 1995).

Anti-nutritional factors in weaner diets

Antigenic components of the diet that cause a delayed hypersensitivity will impose immuno-pathological damage to the small intestine (Miller et al., 1983). Studies by Dunsford et al. (1989) and Dréau et al. (1994) reveal that antigenic soy protein in weaner diets has a stronger effect on gut structure than skim milk protein. Immunologically-active soybean proteins such as glycinin and β-conglycinin stimulate a localized immune response which may result in villous atrophy, crypt hyperplasia and increased serum anti-soy IgG titres (Li et al., 1990; 1991a ; 1991b). These authors also report a reduced growth rate of the piglets, however, any long-term effects of soybean meal on daily gain have not been reported, which indicates that the pigs became systematically tolerant to soy protein some weeks after weaning (Heppell et al., 1989; Wilson et al., 1989). Friesen et al. (1992) conclude that the exclusion of soybean meal from weaner diets will initially have no deleterious effect on gut structure and growth rate. However, these effects may occur when soybean meal is included in the diet at a later stage, for example at 14 days after weaning.

The beneficial effect of creep feeding in supporting immune tolerance after weaning, as was demonstrated by Nabuurs (1993), is disputed. According to Miller et al. (1983), a high intake of creep feed supports immune tolerance whereas a low intake reduces immune tolerance and predisposes the weaned piglet to diarrhea. In contrast, Kelly et al. (1990) reported no effect on gut structure and brush border enzyme activities in weaned piglets fed either no creep feed, or a low or a high level for six days prior to weaning at 14 days of age. According to Pluske et al. (1996b; 1996c) these discrepancies may be due to possible interactions between soybean protein and the level of feeding after weaning *per sé*. Since villous atrophy and crypt hyperplasia are also influenced by level of feeding after weaning (Kelly et al., 1991c, Pluske et al., 1996b, 1996c), the precise contribution of antigenic soybean protein on these indices of gut function cannot be predicted from studies of Li et al. (1990; 1991a; 1991b) and Dréau et al. (1994). These authors reported a

localized immune response induced by immunologically-active soybean proteins but they did not provide informations on the level of feed intake. In conclusion, hypersensitivity reactions to dietary antigens as major cause for changes in gut structure and function and a reduced digestive and absorptive capacity remain to be confirmed.

Tannins which are predominantly present in grain-legumes such as beans (*Phaseolus vulgaris*) and peas (*Pisum sativum*) stimulate endogenous nitrogen loss in piglets suggesting an increased production of mucus (Jansman et al., 1993). However, van Leeuwen et al. (1995) found no differences in villous height, crypt depth, microvilli length and sucrase-isomaltase activities between a low- or high-tannin diet but reported a decreased activity of aminopeptidase in pigs fed the high-tannin diet. This may partly explain the reduction in ileal protein and amino acid digestibilities as was reported by Mosenthin et al. (1993).

The carbohydrates of the glycocalyx, of which the composition changes during maturation of the small intestine, provide a large surface area for interaction between dietary lectins and the intestinal wall (Kik, 1991). Since lectins have different sugar affinities, binding of lectins to the surface receptors on the intestinal epithelium will depend on the stage of maturation of the epithelial cells (Huisman and Jansman, 1991). The binding of lectins to enterocytes interferes with nutrient digestion and absorption (Pusztai, 1989) which can be partly ascribed to mucosal atrophy and reduced enzyme activities as was demonstrated for lectins from *Phaseolus vulgaris* in diets for weaned piglets (Kik, 1991).

Although dietary fiber is mainly fermented in the large intestine, it initially passes through the small intestine. General effects of dietary fiber on the function of the small intestine can be ascribed to (a) higher secretion rate of gastric, biliary and pancreatic juice, (b) mechanical erosion of the mucosal surface leading to an increased loss of endogenous materials (eg. amino acids, minerals) and (c) adsorption of nutrients to fiber. This will result in a decreased absorption of nutrients, especially for amino acids and minerals. Other factors such as meal viscosity and transit time may also be involved.

There is growing evidence that dietary fiber may also modify the morphology of the small intestine, affecting appearance, villi length and number, cell proliferation, mucosal cell division and absorptive function. For example, feeding cellulose to pigs before weaning reduced the villous length by approximately 15% in the jejunum and ileum (Jin, 1992). In studies by Jin et al. (1994) newly-weaned piglets were fed either a high- or low-fiber diet. Although no difference in villous length was obtained in this study, increased depth of crypts was observed in the jejunum and ileum of piglets fed a high-fiber diet. Because the crypts are the principal site of cell proliferation in the intestinal mucosa, these observations, in conjunction with the increased rates of cell proliferation and cell death, support the hypothesis that dietary fiber may increase the turnover rate of intestinal mucosal cells of the small intestine. The specific attributes of fiber that influence these processes are not well known. Furthermore, it can be speculated that dietary fiber reaching the large intestine may also affect the morphology of the small intestine via the influence of short chain fatty acids. For example, n-butyrate circulates following absorption into different organs such as the pancreas and stimulates the production of various messenger molecules such as insulin which, in turn, stimulates gut growth and development Gálfi and Neogrády (1996).

It is well recognized that the gastrointestinal mucosa readily adapts to changes in the level of feed intake. As has been reviewed by McCormack and Johnson (1991), mucosa that does not receive luminal contents becomes hypoplastic and the activities of enzymes associated with growth and proliferation fall to basal levels. However, refeeding results in an increase in the activities of these enzymes and growth and proliferation of the mucosa resume.

In the period immediately after weaning piglets usually fail to consume sufficient feed to cover their energy requirement for maintenance. Le Dividich and Herpin (1994) concluded from data in the literature that the metabolisable energy requirement for maintenance is not met until the fifth day after weaning. McCracken and Kelly (1984) suggest that mucosal atrophy after weaning may be related more to an insufficient level of feed intake rather than to any antigenicity in the diet or to inherently low levels of digestive enzyme activities.

Recent studies by Kelly et al. (1991c) and Pluske et al. (1996b; 1996c) confirm that feeding piglets continuously (as opposed to restricted) after weaning stimulates mucosal growth and function which, in turn, may preserve the integrity of the small intestine and promote growth through an increased digestive and absorptive capacity. In addition, increases of mucosal growth, villous height and crypt depth were associated with high levels of enteroglucagon in plasma of piglets fed continuously (Kelly et al., 1991c). Although it has not been demonstrated until now that exogenous enteroglucagon may stimulate mucosal growth, these results suggest

trophic effects of enteroglucagon in the intestinal mucosa. Kelly et al. (1991c) conclude that increased secretion of this hormone may be the mechanism that influences intestinal adaptation in response to the level of luminal contents (feed intake). Finally, Pluske and Williams (1996) assume that changes in gut structure and function that were originally related to physiological stress imposed on pigs at weaning are most likely confounded with a low feed intake after weaning rather than a consequence of physiological stress *per sé*. In conclusion, the contribution of feed intake *per sé* on morphological and biochemical changes in the small intestine of piglets at weaning needs to be substantiated. Furthermore, possible interactions with other factors as described above that may affect postweaning changes in the structure and function of the small intestine have to be elucidated before strategies can be developed to overcome the postweaning "growth check".

Large intestine physiology

It is well recognized that the principal function of the large intestine is (a) to reabsorb water and electrolytes secreted into the digestive system during digestion, (b) to provide a route for the excretion of waste products of metabolism and of toxic substances and (c) to provide an environment for the complex microflora that concludes the digestive process by fermentation. Although the digestion and absorption of nutrients is very efficient in the small intestine, the large intestine plays a unique role in digestion and utilization of residues that were not digested and absorbed in the small intestine. These residues consist of dietary components such as non-starch polysaccharides, but also of host enzymes and desquamated mucosal cells of the gut. The transit time of digesta is much longer through the large intestine (20-40 h) than through the stomach and small intestine (2-16 h) (Low, 1993). A major consequence of the slow passage rate of digesta through the large intestine is that it encourages prolific bacterial growth. It is well recognized that microbial species produce enzymes such as cellulases, hemi-cellulases, pectinases and others capable of degrading non-starch polysaccharides whereas mammals do not have these enzymes. This part of the review reflects particular interests in specific aspects of microbial function in the large intestine.

Microbial population

The fermentative function of the large intestine is carried out by a rich and diverse population of obligate anaerobic bacteria and, in addition, by some aerobic and facultative microorganisms. The density of the microbial population in the caecum and colon amounts to 10^{10} - 10^{11} viable counts / g digesta, comprising more than 500 different species (Moore et al., 1987). The most dominant Gram-negative species in the ceacal flora were identified as *Prevotella* (*Bacteroides*) *ruminicola* (35%), *Selenomonas ruminantium* (21%) and *Butyrivibrio fibrisolvens* (6%) (Robinson et al., 1981). The Gram-positive species were identified as *Lactobacillus acidophilus* (7, 6%), *Peptostreptococcus productus* (3%) and *Eubacterium aerofaciens* (2, 5%). This is in contrast with the fecal flora in which Gram-positive species including Streptococcus and Eubacterium made up 90% of the flora (Salanitro et al., 1977). These results were similar to those obtained from the colon (Russell, 1979) and agree with data from Moore et al. (1987) who found that the most common isolates in feces were in the Streptococcus genus and represented 27, 5% of all isolates.

There is evidence that the microbial population adapts to the potential substrates which enter the caecum and colon. Varel et al. (1984) report that the numbers of cellulolytic bacteria were increased after prolonged feeding of high-fiber diets. However, this effect appears to be dependent on the source of fiber, because no increase in cellulolytic bacteria was observed when a 20% corn cob diet was fed; however, there was a 200% increase when diets containing 40 and 96% alfalfa meal were fed (table 3). Varel and Pond (1985) conclude that cellulolytic bacteria may represent approximately 10% of the culturable flora when high-fiber diets are fed. The

Table 3. Number of cellulolytic bacteria from fecal samples of sows fed diets containing various levels of fiber[a]

Days on diet	Cellulolytic bacteria ($\times 10^8$ / g of dry wt) in the following diets			
	Control	20% Corn cobs	40% Alfalfa	96% Alfalfa
0	14.7	6.0	10.8	14.1
5	10.1	10.2	34.4	56.5
14	22.4	17.5	18.8	24.2
21	28.4	16.9	41.3	71.0
35	27.8	16.3	105.3	54.9
49	24.6	32.8	43.5	76.3
70	25.0	9.3	56.5	59.3
98	33.3	12.5	50.2	63.7
overall	23.3[c]	15.7[c]	45.1[d]	52.5[d]

[c,d] Means with different superscripts differ ($p < 0.05$).
[a] Adapted from Varel and Pond, 1985.

number of hemicellulolytic bacteria in the colon of pigs also increase when a 40% alfalfa meal diet is fed. *Prevotella* (*Bacteroides*) *ruminicola*, which hydrolyse and utilize larchwood xylan, was the predominant isolate from fecal samples (Varel et al., 1987). Liebler et al. (1992) conclude that the microflora as a whole has a trophic effect on the epithelium. In addition, it provides a continuous stimulus to the local lymphoid tissue and protects against pathogenic species of bacteria which have to compete with the indigenous microflora for nutrition and binding sites.

Factors regulating fermentation

Although the control of fermentation in the large intestine lies beyond the normal regulatory and hormonal mechanisms that modulate other metabolic processes in the body, the host animal has some control over fermentation because diet composition has a major effect on the amount and composition of residues that pass into the large intestine. The main potential substrates for fermentation are different carbohydrates such as (resistant) starch, unabsorbed sugars, raffinose, stacchyose, polydextrose and modified cellulose but also proteins of exogenous and endogenous origin as well as intestinal glycoproteins and mucopolysaccharides (Cummings and Englyst, 1987). By varying diet composition it is thus possible to control not only the activity and the composition of the microflora but also the level and composition of the resulting fermentation products. The pattern of fermentation and the concentration of fermentation products in the large intestine depend primarily on the type and amount of fermentable substrates and the presence of nitrogen, minerals and vitamins that are essential for the overall nutrition of the microbial population. In addition, the growth rate of bacteria is determined by the availability of substrates that are present in the different segments of the large intestine (Bach Knudsen et al., 1993b). These authors demonstrated that bacteria in the cecum and proximal colon, where dietary residues enter the large intestine, have a much higher growth rate than those located more distally. Beyond the descending colon, however, carbohydrates become a limiting factor for the growth of the microflora which then ferment proteinaceous material to a larger extent. Some of the products formed during fermentation of protein such as ammonia, amines, phenols and indols may have negative effects on the health of the epithelial cells (Bingham, 1990).

Fermentation products

Bacteria in the large intestine metabolize carbohydrates to obtain energy for their own growth and maintenance. The final microbial fermentation products are short chain fatty acids (SCFA), which mainly include acetate, propionate and butyrate, and H_2, CO_2 and CH_4. Although methanogenesis in the large intestine is positively correlated to fiber intake (Jensen and Jrgensen, 1994), energy lost as methane from fermentable carbohydrates accounts only for a minimal loss of digestible energy in growing pigs (Christensen and Thorbek, 1987) and sows (Müller and Kirchgessner, 1987). Furthermore, only small net amounts of H_2 are present in the large intestine which indicates that hydrogen sinks other than methane production are involved in H_2-removal (Jensen and Jrgensen, 1994). The SCFA are rapidly absorbed from the large intestine, thus conserving energy and reducing the osmotic load. According to Yen et al. (1991) SCFA may provide up to 30% of the maintenance energy requirements for growing pigs. It is well recognized, however, that energy losses in the form of H_2, CH_4 and fermentation heat as well as the lower efficiency of SCFA utilization by the pig make this route energetically less efficient than utilization of glucose that derives from digestion of carbohydrates by host enzymes in the small intestine. The SCFA are present in the large intestine of pigs at levels ranging from 150-250 mM as opposed to 5-40 mM in the stomach and small intestine (Low, 1993). As predominant anions in the large intestine SCFA create a slightly acidic pH level (Bugaut, 1987), whereas lactic acid as an intermediary product of carbohydrate fermentation accumulates only if SCFA production is inhibited in an acidic milieu of pH less than 5.5 (Soergel, 1994). There is growing evidence in the literature that the type of SCFA formed depends on the composition of carbohydrates available for fermentation. For example, Annison and Topping (1994) showed that SCFA concentrations were increased by feeding diets containing higher levels of non-starch polysaccharides, with acetate to predominate followed by smaller amounts of propionate and butyrate (Low, 1993). In general, as the fiber content of the diet increases, the proportion of acetate to the other SCFA increases (Kass et al., 1980, Stanogias and Pearce, 1985). Special attention has been directed to dietary factors that stimulate the production of butyrate since this acid appears to be one of the factors protecting against colorectal cancer (Bingham, 1990). Studies by Bach Knudsen et al. (1993a; 1993b) reveal that feeding oat bran resulted in a higher proportion of butyrate in large intestinal content compared with oat flour, and that arabinoxylan was responsible for the enhanced butyrate production. In addition, fermentation of potato starch compared to maize starch yields higher proportions of

butyric acid (Mason and Just, 1976)

The SCFA are important for the functions of the large intestine and for the maintenance of the morphological and functional integrity of the colonic epithelium in particular:

- SCFA have been shown to enhance sodium absorption, butyrate being more effective than acetate or propionate (Roediger and Moore, 1981).
- Proliferation of intestinal mucosa in the large intestine is related to the presence of dietary fiber and SCFA (Fleming et al., 1992, Jin et al., 1994). These authors suggest that dietary fiber likely influences intestinal cell proliferation through several interactive mechanisms some of which include luminal factors.
- Butyrate is preferentially metabolized by the colonocytes and accounts for about 70% of the total energy consumption of the colon (Smith and German, 1995) and, in addition, a selective antimicrobial effect of n-butyrate by enhancing the numbers of Lactobacilli and decreasing the numbers of *E. Coli* is suggested (Gálfi and Neogrády, 1996). Since epithelial cells in the large intestine rely for metabolism on SCFA obtained from anaerobic fermentation, the role of SCFA and butyrate in particular as biologically active molecule regulating possible interactions between diet, gut, microorganisms and host warrants further investigations.

There is substantial evidence to show that fermentable substrates available for microbial digestion in the large intestine of pigs increase fecal nitrogen output resulting from an increase in bacterial nitrogen assimilation. The quantitative significance of these processes is shown by the presence of 50 to 90% of bacterial nitrogen in feces (e.g. Sauer et al., 1991, Mosenthin et al., 1992b). It is concluded that the increase in the loss of fecal nitrogen resulting from the dietary inclusion of fiber or non-fibrous carbohydrates cannot be exclusively attributed to interference with protein digestion caused by the bulk of fiber *per sé* and (or) by an increase in rate of passage. It is evident that a more subtle influence on bacterial metabolism is involved. Studies by Mosenthin et al. (1992a; 1992b) reveal that not only undigested dietary protein and amino acids but also endogenous urea secreted into the small intestine may enter the large intestine to be degraded mainly to ammonia. Provided that a fermentable energy source is made available to the bacteria in the large intestine, ammonia is used for *de novo* synthesis of bacterial protein instead of being absorbed. As a result, there is an increase in fecal nitrogen excretion. However, retention of the pigs is not affected since this increase is compensated by a reduction in urinary nitrogen excretion. Similar fundings were reported by other authors (e.g. Misir and Sauer, 1982). A reduced ammonia absorption from the large intestine into the circulation, as a result of increased bacterial assimilation of nitrogen, will save metabolic energy to the animal. Less ammonia would then become available for conversion to urea, a process that requires expenditure of metabolic energy.

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