Parbery, P., & Wilkinson, R. (2012). Victorians' attitudes to farming. Department of Environment and Primary Industries

Williams, P., Gill, A. and Ponsford, I. (2007). Corporate social responsibility at tourism destinations: Toward a social license to operate. Tourism Review International, 11(2), 133-144.

UNDERSTANDING GUT DEVELOPMENT IN THE PIG AND IMPLICATION FOR HEALTH AND NUTRIENT UTILIZATION

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SUMMARY

The gastrointestinal tract (GIT) becomes the primary mode of nutrient digestion and absorption immediately after birth. The GIT must develop capacity to digest and absorb nutrients from feed materials, starting from ingestion of nutrient and immunoglobulin-rich colostrum in the first few days of life of the pig. The pig GIT must also develop capacity to filter of harmful disease causing organisms. Thus, development of adequate gut immunity is essential to the health and optimal utilization of nutrients as well. The microbiome plays a major role in optimal functioning of the gut for nutrient digestion and absorption and immunity. Therefore, development of a robust, diverse and mature gut microbiome is essential developmental process in the growing pig. The continued industry-wide push to limit antibiotic use in swine production may lead to reduced growth performance due to potential loss of the growth promoting effects of antibiotics. Pigs may also become exposed to higher pathogen load. In addition, weaning induces nutritional stress on the pig as it transitions to consumption of solid feed and the stress of independent living away from the sow. Therefore, a better understanding of factors that help to optimize gut development will help to limit the potential reduction in pig performance from complete antibiotic withdrawal from feed.

1.0 Introduction

The digestive tract serves as the entrance for nutrients into the body. It is also a protective barrier, especially against harmful pathogenic organism and compounds into the body. The mouth, pharynx, esophagus, stomach, small and large intestines, cecum, colon, and rectum make up the pig's digestive tract. In addition, the accessory digestive glands (salivary glands, liver, and pancreas) play important roles in the digestive and absorptive process. The small intestine comprises of the duodenum, jejunum, and ileum, which make up approximately 5, 90, and 4 % of the total length

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1.0 Introduction

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The process of feed ingestion in the pig is typical of other animals. Feed is ingested through the mouth and it is mixed with saliva secreted from several salivary glands (parotid, mandibular, and sublingual salivary glands; Yen, 2001). These secretions are important for food lubrication and contain amylase, which helps in the digestion of starches. Feed enters the stomach through the esophagus where it is met with hydrochloric acid and proteases that initiate protein digestion (Yen, 2001). The feed leaves the stomach for the proximal small intestine where it is mixed with bile and pancreatic juice from the acinar regions of the exocrine pancreas (Yen, 2001). The pancreatic juice contains carbohydrases, proteases and amylases that help in the breakdown of proteins, carbohydrates and lipids. Products of digestion are absorbed through various passive, active, and facilitated nutrient transporters that exist on the apical and basolateral surface of epithelial cells, which allow nutrient transfer from the luminal brush border membrane to vascular systems, tissues, and organs. The distal end of the GIT contains the cecum and the colon and these sections account for up to 30 to 60 % of the total intestinal tract. In the adult pig, intestinal contents reside in the large intestine for about 20 hours compared to 2 to 6 hours in the small intestine (Low and Zebrowska, 1989). Significant microbial fermentation of carbohydrates and proteins takes place in the large intestine leading to production of short chain fatty acids (SCFA) or volatile fatty acids (VFA). The VFA serve as a source of energy for the enterocytes and other organs. Furthermore, the large intestine serves a critical role in passive and active reabsorption of water and electrolytes, respectively (Yen, 2001). Development of a robust microbiome helps the pig to ferment the indigestible materials but also helps develop an effective gut immunity. Two critical periods in the life of the pig (the immediate period after birth and after weaning) are associated with drastic changes to digestive physiology. A well-developed GIT is necessary for optimal health and growth efficiency in pigs (Yen, 2001).

2.0 Structural and Functional Development of the Gastrointestinal Tract in the Perinatal Period

The maturation of important GIT functions in the pig occurs just before birth and in the immediate perinatal period (Reeds *et al.*, 1993). After birth, the pig GIT undergoes rapid development due to reliance on oral consumption of nutrients for the first time for its nutrition. Thus, the normally developing pig is able to transition from placental nutrition (parenteral) to full-fledged enteral nutrition (oral) within a very short peri-natal window. Although several factors are involved, elevated cortisol levels at the time of parturition is thought to play a major role in the stimulation of functional maturation of GIT (Trahair and Sangild, 1997; Silver and Fowden, 1989; Sangild *et al.*, 1994a). The different sections of the GIT develop at different rates.

The weight of the stomach increases by about 25% to reach its maximal weight relative to body weight at 1 week after birth. The weight of the pancreas increases very rapidly after birth, and within the first postnatal week its relative weight is 60-80% higher than at birth. The growth of the small intestine is very rapid after birth and within 24 hours after birth, its relative weight could be about 50% higher than at farrowing.

Feeding plays a major stimulatory role of gut development after birth. Enteral intake of colostrum, milk formulas or even elemental diets plays major role in this (Widdowson *et al.*, 1976; Park *et al.*, 1998; Burrin *et al.*, 2000). The study by Widdowson *et al.* (1976) shows a greater growth of the pancreas and small intestine in animals fed colostrum versus fasted. Pigs fed intravenously had decreased intestinal weight in pigs fed through intravenous route versus those orally fed. Neonatal nutrition (milk or colostrum) provides protein, fat and trophic factors such as hormones and growth factors (IGF-I and IGF-II, epidermal growth factor EGF and GLP-2) (Xu *et al.*, 1994; Burrin *et al.*, 1996; Park *et al.*, 1998, 1999; James *et al.*, 1987). For example, exogenous GLP-2 has a significant effect on mucosal growth after birth. Maturation of the stomach at birth leads to increased HCl production. Gastric fluid pH is 2-4 in unsuckled newborn pigs (Sangild *et al.*, 1994b, 1995a). However, mature stomach function is only achieved after 5 days postnatal (Sangild *et al.*, 1992). In addition, gastric protease activity develops rapidly during the perinatal period (Sangild *et al.*, 1991) and the activity of these proteases is dependent on the low pH of the stomach.

Consumption of colostrum stimulates development of activity of brush-border digestive enzymes such as lactase, maltase and aminopeptidases (Sangild *et al.*, 1996; Wang and Xu, 1996; Zhang *et al.*, 1997; Thymann *et al.*, 2006). Furthermore, colostrum consumption is partly responsible for the drastic maturation changes in mucosal structure and production of functional brush-border enzymes (Dudley *et al.*, 1996). Enteral feeding appears to be a crucial factor in the stimulation of production of many enzymes (e.g., aminopepdidase A and dipeptidyl peptidase IV) (Sangild *et al.*, 2000), and certain intestinal nutrient transporters. Post-natal uptake of amino acids and glucose increase dramatically as the microvillus membrane matures (Zhang *et al.*, 1997). For example, parenterally fed 1-week-old pigs have much lower uptakes of glucose and leucine than those fed orally. However, the ability to produce pancreatic and brush border enzymes is not fully developed until 3 to 4 weeks of age (Pluske *et al.*, 1997).

The neonatal pig is also able to absorb intact immunoglobulins to support its passive immunity (Rooke and Bland, 2002). The immunoglobulins are taken up by the process of pinocytosis in which intact large molecular weight proteins are absorbed and transported across the intestinal epithelium into the blood stream. However, pinocytosis stops within 48 hours after birth due to intestinal closure (Weström *et al.*, 1984). Therefore, it is essential that the newborn piglet is able to consume sufficient colostrum during this period to enhance its chance of survival. Unfortunately, about 11-13 % of live born piglets born die before weaning in Europe and North America (British Pig Executive, 2011) and about 50% of the mortality happen in the first week of life (Alonso-Spilsbury *et al.*, 2007; Hales *et al.*, 2014). Increased litter size and competition for feeding means that only the strongest piglets are able to get adequate nutrition and the weak or smallest members of the litter are at a higher risk of inadequate nutrition, disease or even death. Due to the pressure for reducing antibiotic use, sows are vaccinated to protect their offspring against diseases through transfer of passive maternal immunity. This highlights the importance of adequate colostrum intake in today's highly prolific pigs (Farmer and Quesnel, 2009; Quesnel *et al.*, 2012). Insufficient colostrum intake is already well established that as a major cause of preweaning mortality (Edwards, 2002; Le Dividich *et al.*, 2005; Decaluwé *et al.*, 2014). Devillers *et al.* (2011) found a preweaning mortality rate of 43.4% in piglets that had a colostrum intake lower than 200 g, but a rate of 7.1% in piglets with a higher colostrum intake. In addition, higher colostrum intake is more beneficial to weaning, intermediate, and finishing weights in piglets with low versus high birth weights (Declerck *et al.*, 2016). The benefits of adequate colostrum and maternal milk intake is not only dependent on the passage of passive immunity, but also on the effect of adequate nutrition on the maturation of the gastrointestinal tract in terms of its digestive and absorptive function and immune protection.

3.0 Gastrointestinal Development and Function in the Weanling Pig

Although the gastrointestinal tract of the piglet undergoes rapid development in digestive, absorptive and immune defense capacity from birth to weaning, the newly weaned pig has a gut that is still very immature. This is further complicated by the exposure of the weanling pig to environmental, nutritional, and psychological stressors that negatively impair GIT function and health and growth performance (Lalles, 2004). The poor feed intake in the weanling pig in the first week post-weaning causes atrophy of intestinal architecture, which leads to a drastic decrease in brush border enzyme activity (Pluske *et al.*, 1997). Post-weaning intestinal damage along with limited intestinal enzyme function in young pigs leads to poor nutrient utilization, and is a major cause of post-weaning diarrhea. Indeed, there is evidence that nursery pigs are prone to over-stimulation of the mucosal immune system (Pie *et al.*, 2004) and weaning-associated stress hormone spikes which may be associated with activation of inflammatory mediators (Moeser *et al.*, 2007; Smith *et al.*, 2010). Recent evidence also shows that weaning-associated gastrointestinal dysfunction is related to breakdown of epithelial cell tight junction proteins (Overman *et al.*, 2012). Therefore, weanling pigs are vulnerable to intestinal barrier destruction, which may partly explain the reduction in growth and impaired health status of many piglets immediately post weaning.

4.0 Postweaning Changes in the Pig Gastrointestinal Tract

Following weaning there is a decrease (up to 75%) in villus height and increase in crypt depth in pigs at 24-h post-weaning (Hampson *et al.*, 1986). This decrease villus height persists for about 5 days. In addition, weaning-induced changes to the intestinal morphology do not begin to recover until 8 days post-weaning. Weaning-induced anorexia could also lead to reduced crypt cell proliferation during the first week post-weaning (Hall and Byrne, 1989). This destruction in intestinal architecture can compromise digestive efficiency. Pluske *et al.* (1997) showed a direct relationship between villus height and brush border enzyme activity. Age also affects production of digestive enzymes independent of weaning. Moughan *et al.* (1992) showed that gastric pepsinogen production increased at 3 to 4 weeks of age. Cranwell (1995) showed that pancreatic trypsin and elastase activity increased at 4 to 6 weeks of age. Zhang *et al.* (1997) showed brush border lactase activity increased from birth to 14 days of age and then decreases with minimal intestinal lactase activity by 40 days of age. Dunsford *et al.* (1990) reported an increase in goblet cell density from birth to 5 weeks of age. However, it is clear that weaning induced anorexia and its destructive effect on the GIT architecture may be related to post-weaning diarrhea, gut dysfunction, and increased susceptibility to enteric disease (Pluske *et al.*, 1997). Therefore, effective nutritional and management strategies are needed to counteract the insult to the digestive tract after weaning.

5.0 Development of Mucosal Immunity in the Pig

An appropriate development of the mucosal immune system in young animals is critical to both immune protection and gastrointestinal function throughout an animal's lifecycle. At birth, piglets are immune deficient and depend on their mother's colostrum to provide immunological protection (Lalles *et al.*, 2007). The mucosal immune system starts to develop in the first week of age, but is not fully developed until about 8 weeks of age (Miller *et al.*, 1994). However, by about 3 weeks of age pigs have a functional yet immature mucosal immune system (Bailey *et al.*, 2005; Lalles *et al.*, 2007). Bailey *et al.* (2005) showed that before 3 weeks of age intracellular lymphocytes poorly respond to mitogens and subsequently there is poor splenic lymphocyte activation and proliferation. McLamb *et al.* (2013) also showed that prior to 18 days of age pigs elicit a poor innate immune response to pathogenic *E. coli*, which subsequently results in enteric disease. Thus, between 3 to 4 week of age pigs may have an over-active innate immune system and are pre-disposed to chronic gut inflammation. A report by Pie *et al.* (2004) showed a transient up-regulation of inflammatory cytokines such as interleukins (IL-1$\beta$and IL-6), and tumor necrosis factor (TNF-α), in all segments of the small intestine 2 days post-weaning. Pie *et al.* (2004) hypothesized that the spike in IL-6 and TNF-α may be a mechanism to recruit and activate innate immune cells in the mucosa. The weanling pigs may not be able to mount an appropriate adaptive immune response and are prone to overstimulation of the innate immune system, which could lead to gastrointestinal dysfunction. Therefore, strategies are needed to combat the undue stimulation of the gastrointestinal immune system in weanling pigs.

6.0 Implications of Weaning Stress on Swine Gut Health

Pigs are susceptible to dietary-induced stress particularly at the time of diet phase change, especially at weaning when pigs abruptly transition from a milk-based to a grain-based diet (Lalles, 2004). Post-weaning stress events induce neuroendocrine changes that are linked to short- and long-term gastrointestinal dysfunction, disease susceptibility, and reduced growth performance (Lalles 2004; Wijtten *et al.*, 2011). Following weaning, poor feed intake is common and this causes the "transient growth check" period, which lasts for 2 to 5 days and is associated with significant loss of bodyweight (Lalles, 2004). Brooks *et al.* (2001) estimated that approximately 50 and

10% of pigs do not consume feed during the first 24 and 48-h post- weaning, respectively, which limits energy consumption and is an etiological factor for gastrointestinal dysfunction and over stimulation of the mucosal immune system (Lalles, 2004). Pluske *et al.* (1997) showed that postweaning villus atrophy ranged from 45 to 75% although crypt depth was only impacted in cases of severe anorexia. Spreeuwenberg *et al.* (2001) showed a decrease in villus height to crypt depth ratio correlated to a decrease in aminopeptidase A and N, lactase, maltase, and sucrose activity. Therefore, a connection exists between post-weaning anorexia, intestinal morphology, and protein and carbohydrate utilization.

A decrease in exocrine pancreatic secretions during the first week following weaning has been observed (Lalles, 2004). Although weaning-induced changes in intestinal morphology begin to recover by 7 to 10-day post-weaning. Early weaning stress causes villus atrophy and increases intestinal permeability (Hu *et al.*, 2013; McLamb *et al.*, 2013). Moeser *et al.* (2007) and Smith *et al.* (2010) show that stress-induced changes in central and peripheral stress mediators are largely responsible for changes in gastrointestinal function during the first several weeks following weaning. An increase in serum and mucosa corticotrophin releasing factor (CRF) is highly correlated with post-weaning inflammation and loss of integrity and recent evidence shows that CRF recruits and activates intestinal mast cells (Smith *et al.*, 2010). Mast-cell release of tryptase and proteases along with TNF-α triggers a cascade of events that leads to mucosal inflammation and tight junction breakdown (Overman *et al.*, 2012). This event may contribute to impairment of tight junction integrity through alteration in expression of tight junction proteins after weaning (Hu *et al.*, 2013).

The work by Pie *et al.* (2004) showed that during the first 2 days post-weaning there is an increase in most inflammatory cytokines that corresponds to transient gut inflammation, and this is associated with excessive post-weaning chloride ion secretion and diarrhea. In addition, Hu *et al.* (2013) showed that early-weaning stress induced TNF-α -dependent MAPK signaling pathways that lead to activation of transcription factors associated with induction of inflammatory mediators and this was associated with increased gastrointestinal permeability. Spreeuwenberg *et al.* (2001) also showed poor post-weaning feed intake induced inappropriate gastrointestinal inflammation that resulted in an increase in the density of mucosal cytotoxic T cells.

7.0 Strategies to Mitigate Postweaning Gastrointestinal dysfunction

Common nutritional strategies to mitigate post-weaning gastrointestinal dysfunction have included dietary supplementation of milk-based products, plasma protein, probiotics, and prebiotics, and plant-based compounds (Lalles *et al.*, 2007). Supplementation of dairy products as a highly digestible source of carbohydrates and AA leads to improvement in nursery pig performance, gut health, and alter gut microbial ecology (reviewed by Thacker, 1999; Lalles (2007). Inclusion of sprayed dried plasma (SDP) in swine diets increases feed intake, stimulates growth factors such as IGF-1, enhances intestinal morphology, and reduces *E. coli*-associated morbidity (Van Dijk *et al.*, 2001; Touchette *et al.*, 2002). The benefits of SDP are thought to be related to their immunoglobulin and AA content (Lalles, 2007). In addition, supplementation of crystalline AA Glu, Gln, Gly, Ala, Arg, and Cys have also been shown to improve

nursery pig performance through enhancement of gastrointestinal function. Glutamine and glutamate are known common metabolic fuel for enterocytes and dietary supplementation has been shown to mitigate post-weaning villous atrophy (reviewed by Lalles, 2007). In addition, Gly and Ala have been shown to enhance porcine gastrointestinal secretory factors (Ewtushick *et al.*, 2000) and dietary supplementation of Arg mitigates post-weaning villus atrophy by serving as a precursor to polyamines (Harte *et al.*, 2003).

8.0 Use of Probiotics/Prebiotics

Chronic inflammation is a significant mitigating factor against optimal health and growth performance of pigs. Pathogens depress performance by impairing nutrient digestion, absorption and utilization, epithelial integrity and function, and diversion of energy from growth to immune related purposes. Because immune activation depresses efficiency of feed utilization and results in depression in productive performance and mortality, there is great interest in identifying probiotic organisms and prebiotic preparations that can protect pigs against common enteric pathogens of pigs and enhance gut health. The importance of the microbiome for the host is accentuated by the fact that there are about 10 times more microbial cells in the gastrointestinal tract of host animals than all of host cells combined (Savage *et al.*, 1997; Bengmark, 2002). There is an enormous diversity of microbes in the gut, composed mostly of bacteria but also yeast (Koneman, 1978; Laubscher *et al.*, 2000). This results in highly complex interactions in the gut within the microbial community and between the microbes and the host.

Prebiotic supplements are known to elicit beneficial changes in intestinal microflora and mucosal immunity (Lalles, 2007). Probiotic supplements have also been well documented to alter microbial ecology, immune dynamics, and morbidity (Lalles, 2007). *Lactobacillus* strains have been shown to reduce *E. coli* pathogenesis in-vivo (Van Nevel *et al.*, 2003 and 2005) and supplementation with live yeast *saccharomyces cerevisiae* results in reduced intestinal inflammation and post-weaning diarrhea (Baum *et al.*, 2002; Taras *et al.*, 2006). Commensal bacteria have been shown to play a critical role in IgA secretion into the gut lumen and maintenance of gastrointestinal homeostasis through immune mechanisms (Mcpherson, 2008).

Probiotics may stimulate growth through mechanisms that include their effects in regulating the immune system. Regulation of the immune system may lead to suppression of the negative effects of chronic immune activation (Kim *et al.*, 2012). In addition, by directly protecting epithelial barriers, probiotics can enhance nutrient absorption (Awad *et al.*, 2010), which may also result in enhanced growth. There is additional evidence that probiotics may stimulate digestive enzyme activities, which may increase nutrient availability in the gastrointestinal tract (Wang *et al.*, 2010).

9.0 Phytochemical Feed Additives as Antibiotic alternatives for Promotion of Gut Health in Pigs

Phytochemical additives are plant-derived products that have bioactive function (Windisch *et al.*, 2008). Recent concerns on inclusion of growth promoting antibiotics in livestock diets has led to renewed interest around phytochemical feed additives which include herbs, spices, essential oils, oleoresins, and purified plant compounds (Windisch *et al.*, 2008). There is an increasing negative view of sub-therapeutic antibiotic use as growth enhancers with consumer groups, retail food chains and natural/organic food activist groups and the government (Castanon, 2007). The European Union has banned the use of antibiotics as growth promoters (EC Regulation No. 1831/2003) to minimize the risks of development of antibiotic resistant organisms that may pose a threat to human health (Khachatourians, 1998). The recent Veterinary Feed Directive in the US is also meant to limit unregulated use of antibiotics in livestock production.

Phytochemicals have been well documented to modulate intestinal microflora, which results in reduced morbidity and improved growth performance (Windisch *et al.*, 2008; Diaz-Sanchez *et al.*, 2015). For example, supplementation of phytochemicals such as carvacol and thymol have been linked to modulation of intestinal microflora and reduced *E. coli* pathogenesis (Manzanilla *et al.*, 2004). In swine and poultry, supplementation of plant-derived compounds can increase intestinal Lactobacillus and Bifidobacteria populations leading to a decrease in intestinal pH and enhanced nutrient utilization (Jang *et al.*, 2004). The phytochemical-induced microbial modulation increases the capacity for nutrient utilization, which has been demonstrated by improved apparent nutrient retention or digestibility in pigs (Cho *et al.*, 2006). The use of tea polyphenols in nursery pigs has been shown to lead to reduced oxidative stress in the intestinal mucosa of pigs following weaning due to dietary supplementation (Zhu *et al.*, 2012). However, phytochemicals can use reduction in appetite in pigs. Supplementation of products containing oregano, thyme, and garlic cause a dose-dependent reduction in appetite in pigs (Holden, 1998; Windisch *et al.*, 2008). Thus, caution has to be exercised when feeding phytochemicals to feed to ensure levels are fed that do not lead to depressed feed intake. In addition, impact of phytochemicals on swine performance are highly variable and general conclusions on efficacy cannot be made (Windisch *et al.*, 2008; Rodehutscord and Kluth, 2002). Other post-weaning strategies have included use of high levels of zinc in weanling pigs (Bouwhuis *et al.*, 2016). Although concerns still remain about the overall implication of excessive release of zinc into the environment from zinc residues in pig manure (Romeo *et al.*, 2014).

10.0 Summary and Conclusions

The digestive tract in the neonatal pig undergoes significant structural and functional changes as it transitions from placental feeding in utero to oral feeding after birth, and to consumption of solid food after weaning. This development not only prepares the gut for efficient digestion and absorption of nutrients, but it also helps ensure that a mature gut immune system is in place. Unfortunately, an immature digestive tract in neonatal pigs is still partly responsible for a large proportion of peri-natal mortality

and pigs and a significant contributor to the post weaning growth check. Unfortunately, there are no easy solutions. For several decades, the swine industry has been over dependent on antibiotic supplementation. The tide has obviously turned against sub-therapeutic antibiotic use and the industry must look for alternatives to antibiotics. However, a thorough understanding of the process of gut development in the neonatal pig will be essential for determining ideal strategies to optimize gut health and pig performance.

References

Alonso-Spilsbury, M., R. Ramirez-Necoechea, M. Gonzalez-Lozano, D. Mota-Rojas, and M. E. Trujillo-Ortega. 2007. Piglet survival in early lactation: A review. J. Anim. Vet. Adv. 6:76-86

Awad, W. A., K. Ghareeb, and J. Böhm. 2010. Effect of addition of a probiotic micro-organism to broiler diet on intestinal mucosal architecture and electrophysiological parameters. J. Anim. Physiol. Anim. Nutr. (Berl.). 94:486-494.

Bailey, M., K. Haverson, C. Inman, C. Harris, P. Jones, G. Corfield, B. Miller, and C. Stokes. 2005. The development of the mucosal immune system pre- and post-weaning: balancing regulatory and effector function. Proc. Nutr. Soc. 64: 451-457.

Baum, B., E.M. Liebler-Tenorio, M.L. Enss, J.F. Pohlenz, and G. Breves. 2002. Saccharomyces L. and Bacillus cereus var. Toyoi influence the morphology and the mucins of the intestine of pigs. Zeitschrift fu¨r Gastroenterologie 40: 277-284.

British Pig Executive. 2011. Pig yearbook 2011. Agriculture and Horticulture Development Board, Kenilworth, UK.

Bengmark, S. 2002. Gut microbial ecology in critical illness: is there a role for prebiotics, probiotics, and synbiotics? Curr. Opin. Crit. Care. 8:145-151.

Bouwhuis, M.A., T. Sweeney, A. Mukhopadhya, K. Thornton, P.O. McAlpine, and O'Doherty. 2016. Zinc methionine and laminarin have growth-enhancing properties in newly weaned pigs influencing both intestinal health and diarrhoea occurrence. J Anim Physiol Anim Nutr (Berl). 2016 Nov 18. doi: 10.1111/jpn.12647.

Brooks, P.H., C.A. Moran, J.D. Beal, V. Demeckova, and A. Campbell. 2001. Liquid feeding for the young piglet. In: M.A. Varley and J. Wiseman, editors, The weaner pig: nutrition and management, CAB International, Wallingford, UK, p. 153-178.

Burrin, D.G., Wester, T.J., Davis, T.A., Amick, S. and Heath, J.P. 1996. Orally administered IGF-I increases intestinal mucosal growth in formula-fed neonatal pigs. American Journal of Physiology 270: R1085-R1091.

Burrin, D.G., Stoll, B., Jiang, R., Chang, X., Hartmann, B., Holst, J.J., Greeley, G.H. and Reeds, P.J. 2000. Minimal enteral nutrient requirements for neonatal intestinal growth in piglets: how much is enough? American Journal of Clinical Nutrition 71:1603-1610.

Castanon, J. I. 2007. History of the use of antibiotic growth promoters in European poultry feeds. Poult. Sci. 86:2466-2471.

Cho, J. H., Y. J. Chen, B. J. Min, H. J. Kim, O. S. Kwon, K. S. Shon, I. H. Kim, S. Kim, and A. Asamer. 2006. Effects of essential oils supplementation on growth performance, IgG concentration and fecal noxious gas concentration of weaned pigs. Asian-australas. J. Anim. Sci. 19:80-85.

Cranwell, P.D. 1995. Development of the neonatal gut and enzyme systems. In: M.A. Varley, editor, The neonatal pig: development and survival. CAB International, Wallingford. Oxon, UK, pp. 99-154.

Decaluwé, R., D. Maes, B. Wuyts, A. Cools, S. Piepers, and G. P. J. Janssens. 2014. Piglets' colostrum intake associates with daily weight gain and survival until weaning. Livest. Sci. 162:185-192. doi:10.1016/j.livsci.2014.01.024.

Declerck I, Dewulf J, Sarrazin S, Maes D. Long-term effects of colostrum intake in piglet mortality and performance. J Anim Sci. 2016 94:1633-43. doi: 10.2527/jas.2015-9564.

Devillers, N., J. Le Dividich, and A. Prunier. 2011. Influence of colostrum intake on piglet survival and immunity. Animal 5:1605-1612. doi:10.1017/S175173111100067X.

Diaz-Sanchez, S., D. D'Souza, D. Biswas, and I. Hanning. 2015. Botanical alternatives to antibiotics for use in organic poultry production. Poult. Sci. 94:1419-1430.

Dudley, M.A., Burrin, D.G., Quaroni, A., Rosenberger, J., Cook, G., Nichols, B.L. and P.J Reeds. 1996. Lactase phlorhizin hydrolase turnover in vivo in water-fed and colostrum-fed newborn pigs. Biochemical Journal 15:735-743.

Dunsford, B.R., D.A. Knabe, and W.E. Haensly. 1989. Effect of dietary soybean meal on the microscopic anatomy of the small intestine in the early-weaned pig. J. Anim. Sci. 67:1855-1863.

Edwards, S.A. 2002. Perinatal mortality in the pig: Environmental or physiological solutions? Livest. Prod. Sci. 78:3-12. doi:10.1016/S0301-6226(02)00180-X.

Ewtushick, A.L., R.F.P. Bertolo, and R.O. Ball. 2000. Intestinal development of early-weaned piglets receiving diets supplemented with selected amino acids or polyamines. Can. J. Anim. Sci. 80:653-662.

Farmer, C., and H. Quesnel. 2009. Nutritional, hormonal and environmental effects on colostrum in sows. J. Anim. Sci. 87:56-64. doi:10.2527/jas.2008-1203.

Hales, J., V. A. Moustsen, M. B. F. Nielsen, and C. F. Hansen. 2014. Higher preweaning mortality in free farrowing pens compared with farrowing crates in three commercial pig farms. Animal 8:113-120.

Hall, G.A., and T.F. Byrne. 1989. Effects of age and diet on small intestinal structure and function in gnotobiotic piglets. Res. Vet. Sci. 47:387-392.

Hampson, D.J. 1986. Alterations in piglet small intestinal structure at weaning. Res. Vet. Sci. 40:32-40.

Harte, R.D., A.K. Shoveller, R.F.P. Bertolo, and R.O. Ball. 2003. Cystine supplementation adversely affects small intestinal morphology. In: R.O. Ball, editor, Proceedings of the 9th International Symposium on Digestive Physiology in Pigs. University of Alberta Publisher, Banff, CA. p. 213-215.

Holden, P.J., J. McKean, and E. Franzenburg. 1998. Botanicals for pigs-garlic. Iowa State University, Swine Research Report.

Hu, C. H., K. Xiao, Z. S. Luan, and S. Jong. 2013. Early weaning increases intestinal permeability, alters expression of cytokine and tight junction proteins, and activates mitogen-activated protein kinases in pigs. J. Anim. Sci. 91:1094-1101.

Jang, I. S., Y. H. Ko, H. Y. Yang, J. S. Ha, J. Y. Kim, S. Y. Kang, D. H. Yoo, D. S. Nam, D. H. Kim, and C. Y. Lee. 2004. Influence of essential oil components on growth performance and the functional activity of the pancreas and small intestine in broiler chickens. Asian-australas. J. Anim. Sci. 17:394-400.

James, P.S., Smith, M.W., Tivey, D.R. and T.J.G. Wilson. 1987. Epidermal growth factor selectively increases maltase and sucrase activities in neonatal piglet intestine. Journal of Physiology 393:583-594.

Khachatourians, G. G. 1998. Agricultural use of antibiotics and the evolution and transfer of antibiotic-resistant bacteria. CMAJ. 159:1129-1136.

Koneman. 1978. Practical Laboratory Mycology, 2nded. The Williams & Willness company, Baltimore.

Kim, J.S., S. L. Ingale, Y. W. Kim, K. H. Kim, S. Sen, M. H. Ryu, J. D. Lohakare, I, K, Kwon, and B. J. Chae. 2012. Effect of supplementation of multi-microbe probiotic product on growth performance, apparent digestibility, cecal microbiota and small intestinal morphology of broilers. J. Anim. Physiol. Anim. Nutr. (Berl.). 96:618-26.

Lallès, J. P., G. Boudry, C. Favier, N. Le Floc'h, I. Luron, L. Montagne, I. P. Oswald, S. Pié, C. Piel, and B. Seve. 2004. Gut function and dysfunction in young pigs: Physiology. Anim. Res. 53:301-316.

Lalles, J.P., P. Bosi, H. Smidt, and C. R. Stokes. 2007. Nutritional management of gut health in pigs around weaning. Proc. Nutr. Soc. 66:260-268.

Laubscher, W. D. F., B. C. Viljoen, and J. Albertyn. 2000. The yeast flora occurring in the trachea of broiler chicken. Food Tech. and Biotech. 38:77-80.

Le Dividich, J., J. A. Rooke, and P. Herpin. 2005. Nutritional and immunological importance of colostrum for the new-born pig. J. Agric. Sci. 143:469-485. doi:10.1017/S0021859605005642.

Low, A.G., and T. Zebrowska. 1989. Digestion in pigs. In: T. Zebrowska, editor, Protein metabolism in farm animals. Oxford University Press, Oxford, UK. p. 53.

Manzanilla, E. G., J. F. Perez, M. Martin, C. Kamel, F. Baucells, and J. Gasa. 2004. Effect of plant extracts and formic acid on the intestinal equilibrium of early-weaned pigs. J. Anim. Sci. 82:3210-3218.

McLamb, B.L., A.J. Gibson, E. L.Overman, C. Stahl, and A.J. Moeser. 2013. Early weaning stress in pigs impairs innate mucosal immune responses to enterotoxigenic *E. coli* challenge and exacerbates intestinal injury and clinical disease. PLOS ONE. 8(4): e59838.

Mcpherson, A.J., K.D. McCoy, F.E. Johansen, and P. Brandtzaeg. 2008. The immune geography of IgA induction and function. Mucosal Immun. 1:11-22.

Miller, B.G., C.T. Whittemore, C.R. Stokes, and E. Telemo. 1994. The effect of delayed weaning on the development of oral tolerance to soya-bean protein in pigs. Br. J. Nutr. 71: 615-625.

Moeser, A. J., C.V. Klok, K.A. Ryan, J.G. Wooten, and D. Little. 2007. Stress signaling pathways activated by weaning mediate intestinal dysfunction in the pig. Am. J. Physiol. Gastrointest. Liver Physiol. 292: G173-G181.

Moughan, P.J., M.J. Birtles, P.D. Cranwell, W.C. Smith, and M.Pedraza. 1992. The piglet as a model animal for studying aspects of digestion and absorption in milk-fed human infants. World Rev. Nutr. Diet. 67: 40-113.

Overman, E.L., J.E. Rivier, and A.J. Moeser. 2012. CRF induces intestinal epithelial barrier injury via the release of mast cell proteases and TNF-a. PLOS ONE. 7(6): e39935.

Pie, S., J.P. Lalles, F. Blazy, J. Laffitte, B. Seve, and I.P. Oswald. 2004. Weaning is associated with an upregulation of expression of inflammatory cytokines in the intestine of piglets. J. Nutr. 134:641-647.

Yen, J. 2001. Anatomy of the digestive system and nutritional physiology. In: A.J. Lewis and L.L. Southern, editors, Swine Nutrition. CRC Press, New York, USA. p. 19-30.

Park, Y.K., Monaco, M.M. and S.M. Donovan. 1998. Delivery of total parenteral nutrition (TPN) via umbilical catheterization: development of a piglet model to investigate therapies to improve gastrointestinal structure and enzyme activity during TPN. Biology of the Neonate 73: 295-305.

Park, Y.K., Monaco, M.H. and S.M. Donovan. 1999. Enteral insulin-like growth factor-I augments intestinal disaccharidase activity in piglets receiving total parenteral nutrition. Journal of Pediatric Gastroenterology and Nutrition 29:198-206.

Pluske, J. R., D. J. Hampson, and I. H. William. 1997. Factors influencing the structure and function of the small intestine in the weaned pig: A review. Livest. Prod. Sci. 51:215-236.

Quesnel, H., C. Farmer, and N. Devillers. 2012. Colostrum intake: Influence on piglet performance and factors of variation. Livest. Sci. 146:105-114. doi:10.1016/j.livsci.2012.03.010.

Reeds, P.J., Burrin, D.G., Davis, T.A. and M.L. Fiorotto. 1993. Postnatal growth of gut and muscle: competitors or collaborators. Proceedings of the Nutrition Society 52:57-67.

Rodehutscord, M., and H. Kluth. 2002. Tierfu¨tterung ohne antibiotisch wirkende Leistungsfo¨rderer. Zuchtungskunde 74:445-452.

Romeo, A., V. Vacchina, S. Legros, and Doelsch, E. 2014. Zinc fate in animal husbandry systems. Metallomics. 6:1999-2009. doi: 10.1039/c4mt00062e. Review.

Rooke, J. A., and I. M. Bland. 2002. The acquisition of passive immunity in the new-born piglet. Livest. Prod. Sci. 78:13-23. doi:10.1016/S0301-6226(02)00182-3.

Savage, D. C. 1977. Microbial ecology of the gastrointestinal tract. Annu. Rev. Microbiol. 31:107-133.

Silver, M. and A.L. Fowden. 1989. Pituitary-adrenocortical activity in the fetal pig in the last third of gestation. Experimental Physiology 74:197-206.

Sangild, P.T., Hilsted, L., Nexø, E., Fowden, A.L. and M. Silver, M. 1994a. Secretion of acid, gastrin and cobalamin-binding proteins by the fetal pig stomach: developmental regulation by cortisol. Experimental Physiology 79:135-146.

Sangild, P.T., Foltmann, B. and P.D Cranwell. 1991. Development of gastric proteases in fetal pigs and pigs from birth to thirty-six days of age. The effect of adrenocorticotropin (ACTH). Journal of Developmental Physiology 16:229-238.

Sangild, P.T., Silver, M., Fowden, A.L., Turvey, A. and B. Foltman, B. 1994b. Adrenocortical stimulation of stomach development in the prenatal pig. Biology of the Neonate 65:378-389.

Sangild, P.T., Hilsted, L., Nexø, E., Fowden, A.L. and M. Silver. 1995a. Vaginal birth versus elective caesarean section: effects on gastric function in the neonate. Experimental Physiology 80:147-157.

Sangild, P.T., Sjöström, H., Norén, O., Fowden, A.L. and M. Silver. 1995b. The prenatal development and glucocorticoid control of brush-border hydrolases in the pig small intestine. Pediatric Research 37:207-212.

Sangild, P.T., Silver, M., Schmidt, M. and A.L. A.L. Fowden, A.L. 1996. The perinatal pig in pediatric gastroenterology. In: Tumbleson, M.E. and Schnook, L. (eds) Advances in Swine in Biomedical Research. Plenum Press, New York, pp. 745-756.

Sangild, P.T., Petersen, Y.M., Elnif, J., Schmidt, M., Buddington, R.K. and D.G. Burrin. 2000. Premature and term newborn pigs differ in their intestinal response to parenteral and enteral nutrition. Gastroenterology 119: A76.

Smith, F., J.E. Clark, B.L. Overman, C.C. Tozel, J.H. Huang, J.E. Rivier, A.T. Blikslager, and A.J. Moeser. 2010. Early weaning stress impairs development of mucosal barrier function in the porcine intestine. Am. J. Physiol. Gastrointest. Liver Physiol. 298: G352-G363.