Invited review: Aspects of gastrointestinal tract growth and maturation in the pre- and postweaning period of pigs

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ABSTRACT: The growth and development of the gastrointestinal tract (GIT) of the young pig, both before and after parturition, is critical for the animal's future growth and development, efficiency of feed conversion to body depots, and, ultimately, its survival. The perinatal development of the GIT encompasses a *prenatal phase*, a *neonatal phase,* and the *postweaning phase,* which is associated with the adaptation of the GIT to utilize solid feed after the piglet is weaned. The consumption of colostrum, initially, and then milk after birth provides nutrients and compounds for piglets that are critically important as stimuli and substrates to the GIT that in turn evoke a suite of anatomical, immunological, biochemical, physiological, and regulatory processes that advance the overall maturity of the GIT. However, at weaning the combined influence of the various stressors imposed causes a hiatus in the growth and development of the GIT, such that the newly weaned pig endures a "growth check" while exposing it to a greater disease and health risk. Low and variable feed intake is a major outcome of the weaning process, but nevertheless, there are numerous nutritional/management interventions producers can implement in an attempt to overcome this major issue. This review summarizes some major aspects of, and influences on, GIT growth, development, and maturation in the pre- and postweaning period of pigs, demonstrating that postnatal influences occur in utero and that evolution of the GIT continues to occur after weaning.

Key words: creep feed, development, gastrointestinal tract, intermittent suckling, pigs, weaning

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INTRODUCTION

The growth, development, and functionality of the gastrointestinal tract (**GIT**) is a dynamic and evolving process that prepares the young pig, both before and after parturition, for its future growth, development, and, ultimately, survival. It is well recognized that events occurring in the perinatal period can have whole-of-life effects on, for example, feed efficiency, profitability, and/or health resilience (e.g., Dunshea et al., 2003; Williams, 2003; Pluske et al., 2005; Morales and Pineiro, 2006); hence, it is critical that factors influencing the GIT are explored and discussed. In this regard, the perinatal development of the GIT can be divided into three phases: the *prenatal phase*, which is characterized by minimal stimulation from the GIT lumen; the *neonatal phase,* which is associated with changes caused predominately by colostrum and milk intake; and the *postweaning phase,* which is associated with marked changes to, and the adaptation of, the GIT to solid feed (Pluske et al., 1997; Zabielski et al., 2008). Weaning also requires adjustment to other stimuli imposed on pigs during this time such as environmental changes, psychological influences, and/or disease challenges.

There is a plethora of journal articles, reviews, book chapters, and books dedicated to this subject in mammals, including the pig. There are also a number of external and internal factors whose impacts on the growth and development of the GIT are well recognized; however, this particular review will not discuss, at least in any great detail, immunological (aside from the immediate postnatal period), microbial, or environmental influences on GIT growth, development, and function. Other papers in this issue will cover these aspects. Rather, the purpose of the review is to discuss more generalized aspects of prenatal and postnatal development of the GIT and, in particular, focus on the periods immediately after birth and weaning as key intervention points for the manipulation of growth, development, and improved production.

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THE PRENATAL PERIOD

The period immediately following birth is clearly a critical time in the whole life of the pig; however, it is to some extent what occurs in utero that determines growth, development, and survival of the neonate. The weight of the fetus increases dramatically from about d 70 of gestation to parturition (McPherson et al., 2004), and this is associated with marked growth and development of the (immature) GIT that is expedited by hormones, growth factors, and luminal factors/products (Xu, 1996; Sangild et al., 2000). Cortisol produced from the adrenal cortex has received most attention in relation to development of the fetal GIT and of other essential organs such as the lungs, liver, kidneys, and brain in pigs because fetal cortisol secretion increases about 10-fold during the final 3–4 wk of gestation as a result of rapid adrenal gland growth and enhanced sensitivity of the adrenal cortex to stimulation by adrenocorticotropic hormone (Silver and Fowden, 1989). This rapid increase coincides with the normal development of gastric function, including increases in stomach acid and gastrin secretion (Sangild et al., 1991) and in certain enzyme activities (chymosin, pepsin, amylase, lactase, aminopeptidases; summarized in Sangild et al., 2000), which have presumably evolved in preparation for the consumption of colostrum and milk after parturition.

Ingestion of amniotic fluid by the fetus also modulates GIT growth and enzyme activities, although its relative influence would appear to be less than that of glucocorticoids (Sangild et al., 2000). Nevertheless, Sangild et al. (2002) elegantly demonstrated, via esophageal ligation (obstruction) in fetal piglets conducted at a stage approximately 80–90% of gestation to prevent fetal swallowing, that aspects of GIT growth and function in late gestation are diminished when luminal fluids were prevented from being swallowed. The authors found that fetuses with ligated esophagi had a lower body weight (20%) and reduced intestinal weight (43%), aminopeptidase A activity (24%), and glucose absorption (27%), while specific activities of lactase, sucrase, and dipeptidyl peptidase IV were increased (40–50%), compared with sham-operated fetuses. Other parameters of GIT function remained unchanged by esophageal obstruction such as the absorption of amino acids and immunoglobulin and activities of chymosin, amylase, trypsin, chymotrypsin, maltase, and aminopeptidase N (Fig. 1).

In the last 3 wk before parturition, the small intestine grows more rapidly than the body as a whole with its relative weight increasing 70–80% (Sangild et al., 1991). This is accompanied by increases in the absorption of nutrients, as measured by the uptake of monosaccharides (especially glucose) and amino acids by the epithelial mucosa; however, as will be discussed

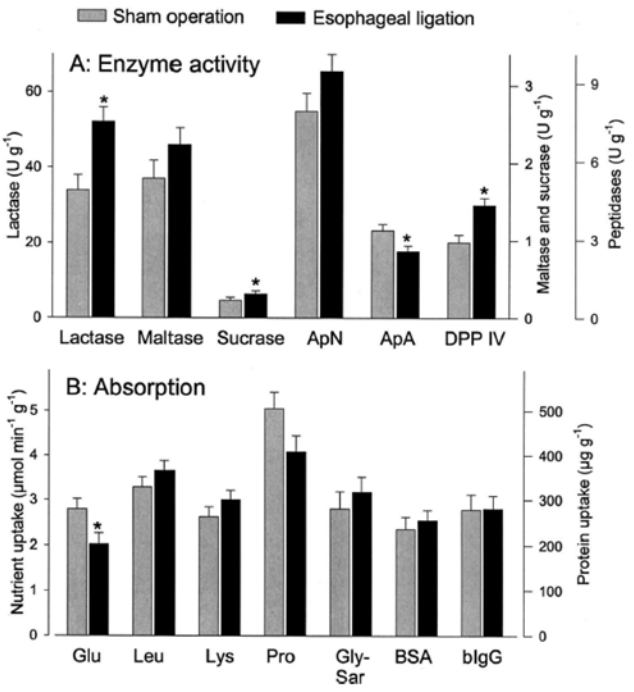

Figure 1. The effects of fetal esophageal obstruction on (A) intestinal activity of lactase, maltase, and sucrase (disaccharidases) and aminopeptidase N (ApN), ApA, and dipeptidyl peptidase IV and (B) intestinal uptake of glucose, leucine, lysine and proline, a dipeptide (glycine-sarcosine), and two protein macromolecules (BSA and bovine IgG). Values are least squares means ± SEM values across the three intestinal segments (proximal, middle, distal; from Sangild et al., 2000).

shortly, a feature of the small intestine of the newborn piglet is its ability to absorb macromolecular proteins such as immunoglobulins across the epithelium into the circulation in the first 24–36 h of birth. Intestinal macromolecule uptake is present in utero during the last 2 wk of gestation but is markedly less in the fetus than in the neonate (Sangild et al., 1999). In contrast to the stomach and small intestine, the prenatal development of the large intestine is less remarkable.

In addition to these events, there is also development of the enteric nervous system (**ENS**) and the neuroendocrine system of the GIT. There are surprisingly few studies in this field in contrast to the vital importance of this physiology to the subsequent growth and survival of young pigs. In one study, Radlowski et al. (2014) investigated the effects of birth weight and diet on the development of the ENS and neuroendocrine system (serotonin, neurotensin, neuropeptide Y) by randomizing newborn small for gestational age (**SGA**) or average for gestational age (**AGA**) piglets into two groups: sow reared (**SR**, 24 h/day with the sow) or formula fed (**FF**, milk replacer). These authors reported that innervation of the colon in SGA piglets was less developed compared to AGA piglets, that serotonin and neuropeptide Y secreting cell numbers increased overtime with the SR compared to the FF diet, and that the distribution of neurotensin cell numbers was highly variable over-

Table 1. The contribution of the selected organs to the total body weight (BW) in landrace × Pietrain crossbred piglets[1]

Item	Suckling neonates (d 0)	Suckling piglets (d 28)
BW, kg	1.45 ± 0.22[2]	8.17 ± 1.22
Small intestine, % of BW	3.10	4.03
Pancreas, % of BW	0.14	0.15
Stomach, % of BW	0.48	0.49
Heart, % of BW	0.76	0.56
Brain, % of BW	2.07	0.59

[1]From Zabielski et al. (2008).

[2]Values are mean ± SD.

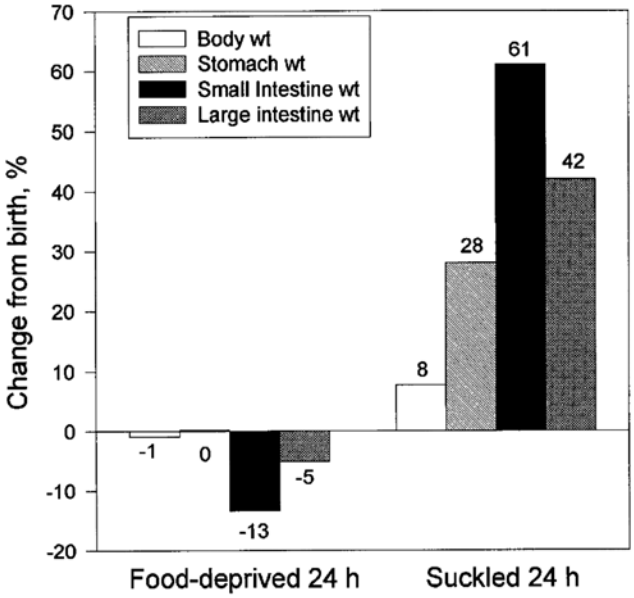

Figure 2. Changes in mass in 24-h suckled piglets compared to food-deprived controls (Widdowson and Crabb, 1976).

time. Birth weight and the type of diet of the neonate clearly influence ENS/neuroendocrine system development, indicating that these physiological functions are compromised in utero and can influence the phenotype. Furthermore, intrauterine growth retardation (**IUGR**), which increases the risk of death of the fetus and the newborn in the perinatal period and can modify/inhibit normal growth and development thereafter, has negative effects on GIT growth and development (e.g., Xu et al., 1994; Wang et al., 2005; D'Inca et al., 2010, 2011). The importance of IUGR to neonatal growth, development, welfare, and survival has received increasing attention of late given the larger litter sizes being produced with hyperprolific sow lines (Campos et al., 2012).

THE POSTNATAL PERIOD

General Growth and Development of the GIT

Once the piglet is born, the GIT must adapt quickly to the transition from parenteral nutrition (via the placenta) to enteral nutrition (colostrum/milk) received per os. Intake of colostrum and milk causes rapid body and organ growth; in the neonatal piglet having an average birth weight of 1.45 kg, for example, weights of the small intestine and pancreas contribute approximately 3.1% and 0.14%, respectively, of the total body weight (Table 1). However, within the first four postnatal weeks the weight of the piglet increases more than fivefold, with the GIT organs growing faster than many other organs of the body (Table 1; Zabielski et al., 2008). In this regard, Widdowson and Crabb (1976) first showed the dramatic rate and extent of changes to body weight and GIT weight, size, and DNA content that occur in naturally suckled, newborn piglets during the first day of postnatal life (compared to counterparts only offered water; Fig. 2). These changes are linked to three major mechanisms, which are increased local blood flow to the GIT with a reduction in basal vascular resistance, accumulation of colostral proteins in enterocytes, and changes in epithelial cell turnover, specifically increased mitosis and inhibition of apoptosis (Zabielski et al., 2008). Numerous subsequent studies have shown that early postnatal growth of the stomach, small and large intestines, liver, and pancreas is disproportionately faster than the rest of body (*positive allometric* growth). For example, the stomach gains 26–28% in weight during the first day compared with a 7–8% increase in body weight during the same period (Widdowson et al., 1976; Xu et al., 1992a). There is also a profound functional maturation of the stomach during the early postnatal period, with gastric acid secretory capacity (expressed per unit of gastric tissue mass) increasing about threefold during the first 3 d of life (Xu and Cranwell, 1990).

In a similar pattern, small intestinal tissue weight increases by up to 70% during the first postnatal day with weight gain primarily confined to the mucosal layer. In parallel, there are rapid increases in small-intestinal length (approximately 20%) and diameter (approximately 15%; Widdowson et al., 1976; Xu et al., 1992b), and the mucosal cell population (as estimated by DNA content) increases by approximately 50% during the first day and doubles by the third day after birth (Xu et al., 1992b). Marked elongation of the villi occurs with the estimated absorption surface area of the small intestine increasing by about 50% during the first postnatal day and about 100% during the first 10 postnatal days in naturally suckled piglets (Smith and Jarvis, 1978; Xu et al., 1992b).

The weight of the large intestine increases by 33% during the first day of life and doubles by the third day, and this weight gain is due to both mucosal and nonmucosal tissue growth. Villus-like structures are observed in the cecum and the proximal colon in piglets at birth and 1 d after birth, but not in piglets 3 d after birth. Xu

et al. (1992a) speculated that such villus-like structures might have a functional significance during the transition to complete dependence on oral nutrition in newborns. In this sense, a primary function of the colon (large intestine) is to absorb water, electrolytes, and short-chain fatty acids (**SCFA**) produced from microbial digestion; however, the retention of dietary carbohydrate through the action of colonic bacteria and production of SCFA relies on inoculation with a microbial population from the sow and environment since the GIT will be sterile at birth. Measurements in the human neonate indicate the small intestine is incapable of hydrolyzing and absorbing all dietary lactose; thus, the colon may play a role in carbohydrate conservation. Murray et al. (1991) studied conceivable routes of colonic energy retrieval from bypass dietary lactose, including mucosal metabolism and absorption as well as bacterial degradation to SCFA and subsequent absorption. Their studies indicated that in the neonatal pig, lactose might be directly absorbed by colonocytes in the disaccharide form.

An important accessory organ of the GIT is the pancreas. The development of the pancreas starts in the prenatal period, and in general, the activity of pancreatic enzymes in tissue homogenates increases with fetal age up to birth. However, it is after birth when there is a positive allometry and an isometry of the pancreas associated with age (Lindemann et al., 1986; Zabielski et al., 1999), and based on DNA and RNA measurements in the pancreas, Corring et al. (1978) ascribed the increase in pancreas weight before 4 wk of age to a hyperplasia of pancreatic cells; subsequent increases involve both hyperplasia and hypertrophy. Lindemann et al. (1986) elegantly showed the ontogenic development of lipase, amylase, chymotrypsin, and trypsin activity of the pancreas from birth to 6 wk of age, with activity (expressed either per gram of pancreas or total activity) increasing linearly to weaning, decreasing in the week after weaning, and then (except for lipase) increasing dramatically thereafter in response to dietary substrate associated with the change from milk to a predominately plant-based diet.

Importance of Colostrum and Milk Composition and Intake

The growth, development, and biological function of the GIT in the postnatal period is determined predominately by the composition and amount of the colostrum and milk the piglet consumes, which in turn impact subsequent growth, development, disease resilience and survival (e.g., Aumaitre and Seve, 1978; Varley et al., 1986; Simmen et al., 1990; Pluske et al., 1995; Le Dividich et al., 2005; Devillers et al., 2011; Quesnel et al., 2012; Theil et al., 2014). Nevertheless, the importance of initial postnatal microbial colonization of the GIT to its subsequent structure and function must also be recognized (e.g., Mulder et al., 2011; Schmidt et al., 2011). A complete description of the various factors impacting colostrum yield, composition, and intake by piglets is beyond the scope of this review; however, from the perspective of the GIT, it is critical that piglets consume colostrum as quickly as possible after birth. The ability of intestinal epithelial cells to take up macromolecules, including immunoglobulins, and to then transport these molecules intact across the epithelium into the blood stream ceases within the first day or two after birth (Sangild, 2003). The efficiency of this process depends in part on the type of diet piglets consume/supplements given, with porcine serum immunoglobulins being superior to bovine immunoglobulins in providing passive immunity to colostrum-deprived piglets (Drew and Owen, 1988; Jensen et al., 2001). Failure by the piglet to consume and absorb sufficient quantities of immunoglobulins impacts negatively not only viability, vitality, and preweaning survival but also future growth and disease resilience.

Colostrum also supplies energy in the form of lactose, fat, and proteins, and it is during the first days of life when sufficient energy intake is crucial because the piglets' energy body reserves, especially fat, are perilously low at birth (Mellor and Cockburn, 1986; Le Dividich et al., 1994; Pluske et al., 1995; Theil et al., 2014). Low energy intake coupled with an inability to thermoregulate can cause morbidity and death (Pluske et al., 1995; Le Dividich et al., 2005; Farmer and Quesnel, 2009; Theil et al., 2014).

Growth Factors in Colostrum and Milk

Colostrum and milk, but especially colostrum, are also rich sources of a suite of compounds such as growth factors, hormones, cells, and antimicrobial factors, including lactoferrin, lysozyme, lactoperoxidase, and cytokines (e.g., IL-1β, IL-6, TNF-α, IFN-γ, and IL-1ra), which in one way or another are involved in the stimulation and regulation of the growth and development of the GIT in this period (e.g., Burrin et al., 1995; Donovan and Odle, 1994; Xu, 1996; Sangild et al., 2000; Xu et al., 2000; Odle et al., 1996; Gauthier et al., 2006; Boudry et al., 2008). It is outside the scope of this review to discuss each (isolated) growth factor/compound and its effects on the structure and function of the GIT for young pigs; however, interest has focused particularly on the properties and roles of epidermal growth factor (**EGF**), the insulin-like growth factors, insulin, and other compounds such as transforming growth factor. Much of this research (and subsequent interest) has been generated by the use of the young pig as a model for human infants and their nutritional needs

and requirements, but nevertheless, some research has been conducted, both before and after weaning, with products (mostly of bovine origin) containing high contents of growth factors and/or immunoglobulins as a source of nourishment and immunity for compromised piglets in the immediate postpartum period (e.g., Drew and Owen, 1988; Muns et al., 2015) and/or in diets for pigs after weaning (Pluske et al., 1999; King et al., 2007; Boudry et al., 2008; van Barneveld and Dunshea, 2011).

Of recent interest with EGF and as an example of biotechnological innovation with potential benefit for young pigs, work conducted at the University of Guelph (Bedford et al., 2012, 2014) has shown that an EGF-containing supernatant, from the culture of a genetically modified EGF-expressing *Lactococcus lactis* (**LL**), can enhance growth performance of early-weaned pigs corresponding to changes in GIT structure and function. In an attempt to unravel potential mechanisms of action, Bedford et al. (2015) used 64 piglets weaned at 3 wk of age and fed them ad libitum one of two treatments for 3 wk: an EGF-containing supernatant from EGF-LL culture (SuperEGF) or a blank M17GE media (Control). The SuperEGF pigs had an increased average daily gain during week 3 after weaning (433 vs. 389 g; $P < 0.05$) and a better overall gain:feed ratio (0.76 vs. 0.68 kg:kg, $P < 0.05$). From a GIT perspective, the structural development of the jejunum was enhanced, and inflammation index was minimized in SuperEGF pigs, as indicated by increased villous height ($P < 0.05$), decreased lamina propria width ($P < 0.05$), and higher expression of the anti-inflammatory cytokine IL-13 ($P < 0.05$). Furthermore, goblet cell numbers and Muc2 levels were increased in SuperEGF pigs. Interestingly, the weaning-induced decrease of glucose cotransporter sodium-glucose linked transporter 1 (**SGLT1**) and glucagon-like peptide-2 (**GLP2**) levels were reversed by SuperEGF supplementation.

In conjunction with work from Zijlstra et al. (1994), for example, showing that high physiological levels of EGF were beneficial in epithelial recovery following rotavirus infection in young pigs, these data provide further evidence of the importance of growth factors, in this case EGF, to the structural and functional integrity of the GIT of the piglet. Arguably, the loss of growth factors including EGF (and immunoglobulins, such as IgG and IgA) has a deleterious temporal impact on GIT structure and function after weaning.

IMPROVING ADAPTATION TO WEANING: EFFECTS ON PRE- AND POSTWEANING STRUCTURE AND FUNCTION OF THE GIT

Weaning of piglets under natural or seminatural conditions occurs over a period of 12–18 wk of age and can be defined as a gradual reduction in the amount of contact between the sow and her piglets, with a concomitant reduction in nursing frequency and milk production and a gradual change of diet from milk to solid or semisolid food(s) (Jensen and Stangel, 1992). In contrast, weaning under commercial conditions is an abrupt separation of the sow from her piglets, resulting in a sudden change in diet, a move to a new environment, and mixing with unfamiliar animals at a much younger age than would occur in natural conditions. Arguably, the primary limiting factor to performance and health directly after weaning is the delay of the initiation of feeding with a concomitant reduction in the consumption of solid food in the week following weaning (Pluske et al., 1997; van Beers-Schreurs et al., 1998; Dong and Pluske, 2007). This, in turn, can cause GIT dysfunction (e.g., Pluske et al., 1997; Lallès et al., 2004; Wijtten et al., 2012) and make pigs susceptible to enteric diseases and/or disorders (Hampson, 1994; Madec et al., 1998). This is compounded by the loss of immune protection provided by sows' milk before weaning.

Low feed intake and the commensurate maladaptation to weaning are caused by a combination of stressors—nutritional, environmental, and psychological—that are imposed abruptly and simultaneously on young pigs in most modern production systems. In one of the few studies to try and partition the relative contribution/importance of these stressors to the postweaning growth check, Funderburke and Seerley (1990) conducted a study with four treatments: 1) control, in which pigs continued to nurse the dam, had access to a dry feed at 14 d of age and were not weaned until after the study (132 h after weaning at d 28 of age); 2) pigs were adjusted to liquid and dry feed at 14 d of age, and sows were removed from the pens at 28 d of age; 3) pigs were adjusted to liquid and dry feed at 14 d of age, and sows were removed at 28 d, but the room temperature was lowered to 13 °C; 4) sows were removed at 28 d but pigs were fed the dry diet only from 28 d of age (summarized in Table 2). The authors reported that pigs having access to milk and dry diets before weaning (treatments 2 and 3) had no adverse symptoms when the sow was removed regardless of whether or not they were exposed to cold after weaning, suggesting that at least maternal separation was of less magnitude than nutritional stress in the postweaning period. However, pigs that were abruptly weaned with a dry diet had slow growth, low plasma glucose, high free fatty acids, and

Table 2. Summary of treatments used to partition the relative effects of different stressors imposed at weaning[1]

	Supplemental diet			Room temperature, °C	
Treatment	Sow removed at weaning (d 28)	Before weaning (at d 28)	After weaning (at d 28)	Before weaning (at d 28)	After weaning (at d 28)
Nursing (1)	No	Dry	Dry	29	29
Weaned (psychological) (2)	Yes	Liquid, dry	Liquid, dry	29	29
Weaned + temperature reduction (environmental) (3)	Yes	Liquid, dry	Liquid, dry	29	13
Weaned + abrupt feeding of dry diet (nutritional) (4)	Yes	None	Dry	29	29

[1]From Funderburke and Seerley (1990).

low liver glycogen. As was surmised by the authors, if the change in eating behavior occurs before weaning (i.e., nursing to eating), then adequate intake of a balanced diet helps reduce the detrimental stress of sow removal or low environmental temperature. In this study, however, pigs remained in the farrowing crate after weaning rather than being moved and mixed into unfamiliar nursery pens. Had mixing and moving of the pigs occurred at weaning, the relative contributions of the different stressors may have been different (Pluske and Williams, 1996; Pluske et al., 1997; Morgan et al., 2014). Nevertheless, methods to stimulate feeding behavior and, by corollary, feed intake directly before and after weaning will assist in amelioration of the "growth check" associated with weaning. Techniques that allow a more gradual change into weaning at an appropriate age may also reduce the impact of the stress response commonly associated with the weaning process; however, before discussion of this part of the review, it is necessary to summarize the major structural and functional changes that occur in the GIT after weaning.

Changes to the Structure and Function of the GIT after Weaning

All components and accessory organs of the GIT are influenced by weaning, irrespective largely of weaning age; however, because of its size and biological importance, it is the small intestine that is affected the most and has to make the greatest anatomical, physiological, and immunological adaptation to changes in the pattern and form of feed consumption, changes in dietary substrates, and adjustment to stress (e.g., Stokes et al., 1994; Cranwell, 1995; Xu, 1996; Pluske et al., 1997; Zabielski et al., 1999; Burrin and Stoll, 2003; Pluske et al., 2003; Boudry et al., 2004; Lallès et al., 2004; Burkey et al., 2009; Wijtten et al., 2011, 2012; Pluske, 2013). It is simply beyond the scope of this review to summarize all the changes to the GIT that occur in the periweaning period, with a plethora of authors having already described the rapid and consistent changes to structure (e.g., villous height and crypt depth, size and shape, tight junction integrity) and function (e.g., digestive and absorptive activity and capacity, loss of surface area, inflammation, antioxidant capacity) that occur in the acute and adaptive phases of growth in the periweaning period (Fig. 3). In more recent times, the profound negative effects of GIT barrier deterioration (small and large intestines) occurring in the immediate postweaning period have become more apparent (e.g., Spreeuwenberg et al., 2001; Moeser et al., 2007a,b; Kim et al., 2012, 2013; Campbell et al., 2013). While feed intake level after weaning affects small intestinal structure and function (Kelly et al., 1991; Pluske et al., 1996a,b), the effect on intestinal barrier function is less consistent, and it is most likely that additional stress (maternal separation, mixing with unfamiliar littermates, and change in environment) coupled with starvation compromises intestinal barrier function (McCracken et al., 1999). In this regard, Moeser et al. (2007b) linked weaning stress and the corticotropin-releasing factor (**CRF**) signaling pathways to GIT dysfunction, demonstrating that weaning (at 19 d of age) caused an immediate breakdown of intestinal barrier function that was characterized by a reduction in transepithelial electrical resistance and increased paracellular [^{3}H] mannitol flux. These changes in the mucosa were mediated by activation of peripheral CRF receptors commensurate with inflammatory responses, mast cell activation, and the release of some proinflammatory cytokines and can be modulated by a delay in the weaning age (Moeser et al., 2007a).

Increasing Dry Matter Intake before Weaning

There have been a plethora of studies dating back decades aimed at increasing the consumption of dry matter before weaning. Supplementary intake of nutrients in the period before weaning is generally provided to litters of piglets in the form of a milk liquid diet, a gruel, and/or a solid ("creep") diet, with piglets being offered a milk liquid diet consuming more dry matter, on average, than piglets offered a dry creep diet or no supplemental feed (e.g., Pluske et al., 1995; Dunshea et al., 1998; Wolter et al., 2002; King and Pluske, 2003; Pluske et al., 1997; Pluske et al., 2005). Nutrients in these forms are offered to piglets before weaning in an attempt to 1) increase daily weight gain at a time when the sows' proportional milk yield relative to piglets'

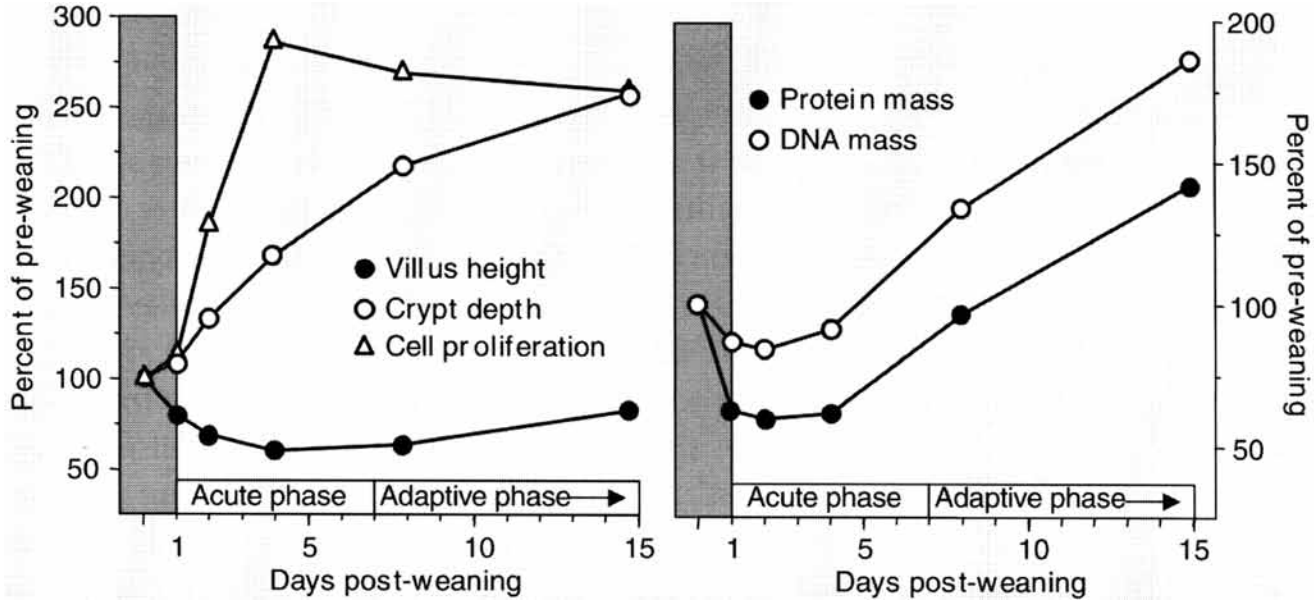

Figure 3. Two phases of change in the small intestine, acute phase and adaptive phase, that occur after weaning (Burrin and Stoll, 2003).

demand for growth is declining and 2) prepare them for the transition to a (solid) diet after weaning.

Creep feeding begins largely as an exploratory and social activity and then becomes more driven by nutrient demand as the pig matures in the fourth or fifth week of age (Pajor et al., 1991); however, it is well documented that creep feed consumption per litter varies immensely (e.g., English, 1981; Pajor et al., 1991; Pluske et al., 1995; Pluske et al., 2007). Furthermore, weaning age can influence intake before weaning, with van der Meulen et al. (2010), for instance, finding that weaning at 7 wk of age (compared to 4 wk of age) in combination with creep feeding improved postweaning feed intake and reduced weaning stress but did not improve functional characteristics of the small intestinal mucosa such as plasma intestinal fatty acid binding protein (a marker for mild intestinal injury) concentrations, intestinal morphology, intestinal (macro)molecular permeability, and intestinal fluid absorption.

In earlier years when it was commonplace to wean at 6–8 wk of age, it was estimated that 50–80% of a piglet's food requirement was obtained from creep feed and the remainder from milk (English et al., 1977; English, 1981). However, as weaning has become earlier, the dietary change(s) at weaning is likely to be greater, and hence, more effort is required to encourage the consumption of food(s) before weaning to minimize the extent of a sudden diet change. A number of studies have now shown that solid feed intake (or disappearance) during lactation may be related to feed intake in the early postweaning period (e.g., Bruininx et al., 2002; Kuller et al., 2004; Berkeveld et al., 2007b), although other studies show the lack of any effects of creep feed disappearance on postweaning performance or only a tendency for an improvement (see Pluske et al., 1995; King and Pluske, 2003). A reason for this variation could be due to the unit of replication for statistical analysis, with, for example, Fraser et al. (1994) demonstrating that a between-litter analysis showed no tendency for litters that had eaten the most creep feed in lactation to gain more weight after weaning, whereas a within-litter analysis showed there was a small but significant tendency for piglets with a high creep feeding score to gain more weight than their littermates after weaning. There is also, quite simply, enormous litter-to-litter variation in disappearance that further complicates these effects.

In this context, Bruininx et al. (2002) examined whether creep feed consumption before weaning stimulated the development of postweaning feed intake and performance of individual weaned pigs. The authors showed that feed intake and growth in the first 8 d after weaning was greater ($P = 0.02$ and $P = 0.01$, respectively) for eaters than for noneaters of creep feed in lactation or piglets not offered any creep feed during this period. Furthermore, the number of visits to the feeder during which feed was consumed was higher for the eaters ($P < 0.05$) than for the noneaters and piglets not offered creep feed, with feeder design and the duration of creep feeding also having an influence on disappearance but not always an increase in growth between different treatment groups (Sulabo et al., 2010a,b). Data, therefore, generally support the notion that enhanced familiarity with solid food at weaning causes the weanling pig to focus more on feed intake and less on exploratory behavior (Bruininx et al., 2002). Other studies (e.g., Kuller et al., 2004, 2007; Pluske et al., 2007; Collins et al., 2013), in which pigs were categorized into eaters and noneaters of creep feed, have generally

shown that only a proportion of pigs within the litter consume creep feed and that eaters have better initial postweaning performance than noneaters.

Intermittent Suckling: A Form of Gradual Weaning

Intermittent suckling (**IS**) is a process whereby piglets are separated from the sow for a specified period of time each day in the latter stage of lactation. This practice not only can induce estrus in lactation with the potential for rebreeding at that time (Downing, 2015) but offers considerable potential benefit for piglets, including an increase in supplementary feed intake (Gerritsen et al., 2008), enhanced familiarization with the maternal separation that occurs at weaning (Berkeveld et al., 2007a), and a more expedient consumption of feed after weaning through greater familiarization with the supplementary feed (Kuller et al., 2010). Previous studies using IS have examined aspects of GIT morphology (Berkeveld et al., 2009) and behavior (Berkeveld et al., 2007a) and linked them to favorable postweaning outcomes. For example, Nabuurs et al. (1993, 1996) provided creep feed through an 8 h daily separation from the sow and observed significantly higher villi and deeper crypts on d 7 and 4 after weaning, respectively, compared to piglets that received no supplementary creep feed. At weaning, crypts were deeper in the pigs that were given supplementary creep feed, suggesting that new villous cells were being produced faster (Nabuurs et al., 1993). Interestingly, total net absorption calculated over 24 h over the entire length of the small intestine showed that pigs fed creep feed absorbed 600 mL more fluid 4 d after weaning and 400 mL fluid 7 d after weaning than pigs that did not receive any creep feed during the suckling period (Nabuurs et al., 1996). However, less attention has been paid to GIT absorptive function associated with IS in the pre- and postweaning periods and any possible negative effects of repeated maternal separation on indices of piglet welfare. Given the previous discussion pertaining to the importance of early onset of feed intake after weaning, the use of IS as a potential management tool will now be discussed in more detail with an emphasis on the GIT.

The majority of studies with IS show an abrupt, initial reduction in growth rate in lactation associated with its implementation due simply to the associated reduction in milk intake from the sow (Thompson et al., 1981; Kuller et al., 2004, 2007; Berkeveld et al., 2007b, 2009). This reduction in growth, however, is less than that observed when piglets are weaned conventionally and is compensated for in the first week after weaning, with pigs subjected to IS in lactation displaying greater feed intake and faster growth (Kuller et al., 2004, 2007; Berkeveld et al., 2007b). Berkeveld et al. (2009) investigated a daily piglet separation of 10 h for 1 or 2 wk with weaning at d 26 or d 33 and reported a marked diminution in the postweaning growth check with the extended lactation. Additionally, subjecting piglets to a longer IS regimen facilitates their adaptation because feed intake was improved shortly after weaning by a longer period of IS during lactation (Berkeveld et al., 2009). However, it has been suggested that the positive effects of IS on performance after weaning may also be mediated by other factors in addition to increased creep feed intake during lactation (Berkeveld et al., 2009; Kuller et al., 2010). Kuller et al. (2007), for example, showed that IS litters consuming little or no creep feed during lactation still tended to have higher feed intake and weight gain after weaning than control litters with a comparable low feed intake during lactation. Additionally, Berkeveld et al. (2009) showed that although feed intake before and within the first 2 d after weaning was not improved with 7 d of IS before weaning (d 26), this did not cause a significant reduction in villous height in comparison to conventionally weaned counterparts.

Moreover, Turpin et al. (2014) examined whether a combination of an extended lactation length to 35 d and IS would increase solid feed intake before and after weaning. These authors found higher growth rates 12 d after weaning and an improvement in GIT absorptive function (as assessed by galactose absorption). However, differences in ADG had disappeared by the time pigs reached 90 d of age. The authors concluded that IS involving an 8 h daily separation the week before weaning did not appear to prevent weaning-associated changes, but rather advanced them in an attenuated way, thereby providing a more gradual transition into weaning that was more pronounced when piglets were weaned at a later age (i.e., 35 d).

As alluded to previously, augmented familiarization with feed and reduced stress associated with maternal separation may have contributed to these changes with IS. Early weaning of piglets (19 d of age), compared to piglets weaned at 28 d of age, activated stress signaling pathways both centrally (in the hypothalamus) and in the GIT that contribute to deteriorated epithelial barrier function (Moeser et al., 2007a). From a behavioral point of view, Berkeveld et al. (2007a) observed piglets on various days until d 37 of an experiment (IS staring at d 19 until weaning at d 41 to 45, with a 12 h separation per day) and concluded that IS was not associated with any behavioral patterns indicative of piglet distress. Turpin et al. (2015) were also unable to find any welfare-related concerns after weaning associated with IS.

To date, it seems that despite the benefits of IS in the initial postweaning period, no differences in body weight or feed intake have been observed at the end of experiments (Kuller et al., 2004, 2007; Berkeveld et al., 2007b,

2009; Turpin et al., 2013). Kuller et al. (2007), for example, measured performance until slaughter and found no significant difference between treatments. However, it has been postulated that these beneficial outcomes may become more prolonged when piglets are weaned under suboptimal conditions, such as on farms with a history of postweaning diarrhea (Berkeveld et al., 2009).

CONCLUSIONS

Before birth, maturation of the fetal GIT is influenced by both luminal stimuli (e.g., swallowed fluid) and hormonal factors (e.g., endogenous cortisol release). During the last weeks before term, the pig GIT grows more rapidly than the body as a whole, and the functional capacity increases for most digestive processes. Organ maturation then occurs rapidly in the perinatal period in association with the transition from placental to enteral nutrition, such that the enteral intake of nutrients from colostrum and milk in newborn piglets causes marked structural and functional changes in the GIT, such as the development of brush-border enzyme activities and increased transporter capacity for absorption. In this regard, the importance of colostrum composition and colostrum intake by the piglet cannot be disregarded given its critical roles in the subsequent growth and maturation of the GIT. Early postnatal growth and development of the GIT is coincidental with changes in the development of the intestinal immune system, with an appropriate expansion of humoral and cellular functions of the intestinal immune system being necessary for subsequent growth, performance, and survival. At weaning and largely independent of weaning age but dependent on diet type, diet form, and the rearing environment (e.g., outdoors vs. indoors), the young pig is subjected to myriad changes (nutritional, psychological, environmental) that further modify the overall structure and function of the GIT. The postweaning period is regarded as critical for the subsequent production and health, and possibly behavior, of pigs through to the finisher phase of growth; hence, much interest has been directed worldwide toward mitigating the postweaning malaise and identifying means (via nutrition, management, disease interventions) to positively influence GIT structure and function to, in turn, enhance production and health outcomes.

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