Weaning Induces Both Transient and Long-Lasting Modifications of Absorptive, Secretory, and Barrier Properties of Piglet Intestine[1,2]

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ABSTRACT This study investigated intestinal physiology of piglets at weaning. Piglets (n = 60) weaned at 21 d were food deprived for 2 d and then tube-fed using 2 different diets (a conventional diet vs. a wheat-enriched diet). They were slaughtered at d 0, 2, 5, 8, or 15 postweaning. Jejunum, ileum, and colon were mounted in Ussing chambers. In addition, segments of the proximal jejunum of 4 growing pigs were studied 35 d after weaning. Secretory function was assessed by basal short-circuit current (Isc) and secretagogue-stimulated Isc. Glucose absorption was measured by the increase in Isc after the addition of glucose. Epithelial barrier function was measured by transmucosal resistance (R) and horseradish peroxidase (HRP) fluxes across the epithelium. There were no significant differences between the pigs fed the 2 diets for any of the parameters studied. As already reported, a transient villous atrophy was observed. At the same time, we observed an increased basal Isc in jejunum and colon, increased glucose absorption and a dramatic drop of R in jejunum. These parameters had returned to preweaning values by d 5. Weaning was also followed by long-lasting modifications. In jejunum, responses to the secretagogues and glucose absorption were decreased at wk 2 after weaning and were not different between d 15 and 35. Ileal transmucosal resistance increased on d 5 and was stable thereafter. HRP flux in jejunum declined on d 2 and stayed at this low level throughout the experiment. We conclude that weaning induces transient dramatic changes in intestinal physiology but is also a period of maturation of the intestine. J. Nutr. 134: 2256–2262, 2004.

KEY WORDS: • *pigs* • *weaning* • *intestinal permeability* • *electrolyte transport* • *glucose absorption*

The development of the mammalian intestine is a highly organized process that results in the formation of a specialized mature epithelium. Intestinal epithelial cells have to fulfill different roles, including classical digestive and absorptive functions, maintenance of a barrier against noxious antigens and bacteria, and secretion of water and electrolytes to keep a proper viscosity of the luminal contents and flush out noxious components (1). Pre- and postnatal phases leading to maturation of intestinal epithelial cells occur in the early life of the animal: morphogenesis and cytodifferentiation in utero preparing the epithelium for digestion and absorption of colostrum and milk components, birth and early suckling corresponding to a dramatic shift from parenteral to enteral nutrition, and weaning of the offspring from mother's milk to a diet largely based on plant products. Although the first 2 phases have been well described in pigs (2), the effect of weaning on absorptive and secretory physiology and intestinal barrier function is not fully understood. Indeed, either only the first 4–5 d after weaning were studied (3,4) or the weaning period was skipped and only comparisons between newborns and fully weaned pigs were performed (5–8). No comprehensive study of the specific weaning period has been conducted so far. However such information would be relevant to the understanding of postweaning diarrhea, especially in the close perspective of a total ban on in-feed antibiotics in the European Union. The aim of our work was therefore to investigate precisely the absorptive and secretory physiology as well as epithelial barrier function of different sites of the intestine of piglets after weaning. Food intake was controlled by using tube feeding and 2 different diets were used to assess possible dietary influences.

MATERIALS AND METHODS

Animals. All experimental procedures were conducted in accordance with the National Institutes of Health Guide and the French Ministry of Agriculture for the care and use of laboratory animals. Large White × Landrace piglets (n = 60) obtained from the INRA

[1] Presented in part at the 9th International Symposium on Digestive Physiology in Pigs, May 14–17, 2003, Banff, AB, Canada [Boudry, G. Péron, V., Lallès, J. P. & Sève, B. (2003) Weaning induces transient and long-lasting modifications of secretory and absorptive physiology of piglets small intestine. In: Proceedings of the 9th International Symposium on Digestive Physiology in Pigs (Ball. R. O., ed.), vol. 2, pp. 121–123 University of Alberta, Edmonton, Canada] and [Boudry, G., Péron, V., Lallès, J. P. & Sève, B. (2003) Development of intestinal barrier function at weaning in piglets. In: Proceedings of the 9th International Symposium on Digestive Physiology in Pigs (Ball, R. O., ed.), vol. 2, pp. 195–197. University of Alberta, Edmonton, Canada].

[2] Supported by a grant from the European Union (EU project QLK5-CT-2000–00522). The authors are solely responsible for the work described in this article, and their opinions are not necessarily those of the European Union.

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0022-3166/04 $8.00
Manuscript received 1 March 2004. Initial review completed 11 April 2004. Revision accepted 3 June 2004.

TABLE 1

Composition of postweaning diets

	Diet 1	Diet 2
	g/kg	
Wheat	243.1	678.9
Barley	245.0	—
Soybean meal	160.0	160.0
Maltodextrin	40.0	—
Whey powder	150.0	—
Soluble fish protein concentrate	82.5	83.0
Sunflower oil	28.0	26.0
Calcium carbonate	15.0	18.0
Monocalcium phosphate · $2H_2O$	20.0	22.0
Sodium chloride	—	2.0
Trace element and vitamin premix[1]	5.0	5.0
L-Lysine · HCl	1.3	2.5
DL-Methionine	8.5	0.7
L-Threonine	1.3	1.6
L-Tryptophan	0.3	0.3

[1] Composition in g/kg: calcium carbonate (excipient) 550.69; zinc oxide (78% Zn) 25.7; copper sulfate (25% Cu) 16.0; manganese oxide (62% Mn) 11.7; iron carbonate (40% Fe) 50.0; calcium iodate (62% I) 0.32; cobalt sulfate (21% Co) 1.9, sodium selenite (1% Se) 6.0; retinol (500,000 IU/g) 4.8; vitamin A/vitamin D-3 (500,000/100,000 IU/g) 1.2; cholecalciferol (500,000 IU/g) 0.96; tocopherol (500 IU/g) 16.0; menadione (22.7%) 1.76; thiamin (98%) 0.4; riboflavin (80%) 2.5; niacin (pure) 6.0; Ca pantothenate (99%) 3.0; pyridoxine (pure) 2.0; biotin (2%) 2.0; folic acid (pure) 0.4; cyanocobalamin (1‰) 10.0; ascorbic acid (pure) 20.0; choline chloride (60%) 266.67.

herd were selected from 18 litters. Piglets were divided into 30 pairs of weight-matched littermates. The experiment was conducted in 6 replicates of 5 pairs each. Each member of the pair was randomly allocated to one of the postweaning diets (**Table 1**).

Piglets were weaned at 21 d of age. At weaning, 3–4 nonlittermates were placed together in metabolism cages for 24 h. They were then surgically implanted with a gastroesophageal tube to allow tube feeding, and placed individually in metabolism cages. All of the piglets were food deprived for 48 h after weaning. They were then tube-fed 1 of the 2 experimental diets [dry matter (DM)[4]:water, 1:2] 6 times daily at 3-h intervals between 0600 and 2100 h. Daily feed intake level was adjusted to the pig's metabolic weight according to a prefixed schedule [linear increase from 8.7 to 71.3 g DM/(d · kg $BW^{0.75}$) from d 3 to 11, then a stable level of 80 g DM/(d · kg $BW^{0.75}$) from d 12 to 15]. In each dietary group, 6 piglets were killed the day of weaning (d 0) and 2, 5, 8, and 15 d postweaning. Caution was exercised to have the same number of heavy (weaning BW > 6.6 kg), medium (5.2 < weaning BW < 6.6 kg) and light (weaning BW < 5.2 kg) piglets for each day and each diet. Piglets were killed 3 h after the last meal except on d 0 when they were killed 1 h after the last suckling period.

Piglets were killed by electronarcosis followed immediately by exsanguination. After laparotomy, a 20-cm segment of the proximal jejunum (beginning 20 cm from the ligament of Treitz), a 20-cm segment of the distal ileum (beginning 50 cm proximal to the ileocecal valve) and a 20-cm segment of the proximal colon (beginning 15 cm from the ileocecal valve) were removed and placed in Ringer's bicarbonate solution (in mmol/L: 145 Na^+, 128 Cl^-, 0.32 PO_4^{3-}, 2 Ca^{2+}, 1 Mg^{2+}, 25 HCO_3^-, 1 SO_4^{2-}, 6.3 K^+; pH 7.4) and immediately mounted in Ussing chambers. Adjacent pieces of proximal jejunal and distal ileal segments (5 cm each) were fixed in buffered formalin (10%) for 24 h at 4°C, then washed and stored in ethanol:water (75:25, v:v). Mucosal scrapings from adjacent jejunum and ileum segments (20 cm each) were prepared and snap-frozen in liquid nitrogen then stored at −80°C until enzyme activity analysis. Segments for Ussing chambers, morphometry analysis, and mucosal scrapings were taken in the same sequence each time.

Measurements of electrical parameters and permeability to horseradish peroxidase. Electrophysiologic properties and permeability to horseradish peroxidase (HRP) of the small intestine and colon were measured in a set of 12 Ussing chambers, as already described (9). Six chambers were used for electrophysiological parameter measurements with 2 chambers per intestinal site (proximal jejunum, ileum, and colon). Tissues were left to equilibrate for 20 min before basal short-circuit current (Isc) and transmucosal resistance (R) were evaluated as the mean values from 20 to 30 min. Glucose absorption was assessed through the increase in Isc (ΔIsc) after mucosal addition of 16 mmol/L D-glucose osmotically balanced on the serosal side by 16 mmol/L mannitol. Secretagogue-induced chloride secretion was studied by addition of 0.1 mmol/L serotonin (5-HT; Sigma) followed 10 min later by 2.2 mmol/L theophylline (Sigma). Six other chambers (2 chambers per intestinal site) were used to measure intestinal permeability to macromolecules using HRP as a model protein, as already described (9).

Small intestine morphology and enzyme activity. Samples for determination of small intestine morphology were microdissected for villi and crypts and measured according to the technique of Goodlad et al. (10). Briefly, specimens were stained with Schiff's reagent after hydrolysis in 1 mol/L HCl at 60°C for 6 min. Bands of villus-crypt units were cut and isolated from the connective tissue, using a fine-gauge syringe needle under a dissecting microscope. The preparation was mounted on a glass slide in a drop of acetic acid (45%). Villous and crypt lengths were measured using an optical microscope (Eclipse E400, Nikon), a camera (Digital camera DXM1200, Nikon) and an image analyzer (Lucia software). Mean values of these parameters were determined for 10 individual villi and crypts from each specimen.

The specific activities of lactase-phlorizin hydrolase (EC 3.2.1.23) and maltase (EC 3.2.1.20) were determined according to the methods of Dalqvist et al. (11) using lactose and maltose as substrates, respectively. The protein content of tissue homogenates was measured using the Bio-Rad protein assay reagent (Bio-Rad).

Additional measurements. To assess whether the changes observed in the jejunum 15 d after weaning were long lasting, we performed an additional set of experiments with four 9-wk-old growing pigs (i.e., 35 d after weaning) from the INRA herd of the experimental unit. They were killed by electronarcosis and exsanguination 3 h after their last meal. A 20-cm segment of proximal jejunum (beginning 20 cm from the ligament of Treitz) was removed after laparotomy. The tissue was mounted in Ussing chambers and studied as described above.

Statistics. All of the data were subjected to ANOVA using the General Linear Model procedure of the Statistical Analysis System (SAS Institute). The effect of diet, time, pair of piglets, and replication were first tested by the Snedecor *F*-test. Because the effects of diet and the diet × time interaction were never significant, diet was removed from the model and only the effect of time and replication were tested by the Snedecor *F*-test. Adjusted means were compared by the Student's *t* test. Jejunal data from piglets 15 and 35 d after weaning were compared by the Student's *t* test. Values presented are lsmeans ± SEM. Differences are considered significant when $P < 0.05$.

RESULTS

Influence of postweaning diet. The pigs fed the 2 experimental diets did not differ in any of the parameters studied and there were no diet × time interactions. Therefore, data from the 2 groups were pooled and only the effect of time after weaning was studied.

Influence of weaning on small intestine morphology and enzyme activity. Villous height in the proximal jejunum decreased by 40% from d 2 to 8. It was still lower at d 15 (77%

[4] Abbreviations used: BW, body weight; DM, dry matter; HRP, horseradish peroxidase; 5-HT, serotonin; IL, interleukin; Isc, short-circuit current; R, transmucosal resistance; VIP, vasoactive intestinal peptide.

TABLE 2

Intestinal architecture and enzyme activity in the small intestine of piglets after weaning[1]

	Site	Day postweaning 0	2	5	8	15	SEM
Villous height, *μm*	Proximal jejunum	597[a]	356[c]	359[c]	377[c]	457[b]	27
	Distal ileum	340	295	268	329	317	20
Crypt depth, *μm*	Proximal jejunum	216[c]	211[c]	367[a]	304[b]	308[b]	13
	Distal ileum	156[c]	146[c]	194[b]	204[b]	240[a]	10
Lactase, *U/mg protein*	Proximal jejunum	59[a]	48[b]	17[c]	17[c]	12[c]	5
	Distal ileum	11.4[a]	3.9[b]	1.7[b]	3.3[b]	1.4[b]	1.5
Maltase, *U/mg protein*	Proximal jejunum	42	37	31	43	43	5
	Distal ileum	29	27	32	48	45	7

[1] Values are lsmeans, $n = 12$. Within a row, lsmeans with superscripts without a common letter differ, $P < 0.05$.

of preweaning value; **Table 2**). Villous height in the distal ileum was not affected. From d 2, crypt length gradually increased with time in the distal ileum reaching values 53% higher at d 15 than at d 0 (Table 2). The same trend was observed in proximal jejunum with a peak in crypt depth at d 5 (Table 2). Lactase specific activity decreased by nearly 90% between d 0 and 5 at both sites, whereas that of maltase was not altered by weaning (Table 2).

Influence of weaning on intestinal secretory capacity In the proximal jejunum and colon, basal Isc increased on d 2 but returned to the preweaning value by d 5 (**Fig. 1***A* and *C*). In ileum, basal Isc switched from positive to negative values. However, these changes were not significant ($P = 0.0775$ for d 8 vs. d 0 and $P = 0.1371$ for d 15 vs. d 0) (Fig. 1*B*).

The response to the neuronal agonist 5-HT and the cAMP agonist theophylline was measured as the increase in Isc after the addition of these substances into the bathing solutions. In proximal jejunum, the response to 5-HT and theophylline decreased in wk 2 after weaning to reach levels at d 15 that were 62% lower than at d 0 (ΔIsc 5-HT, $\mu A/cm^2$: 198 ± 32 at d 0 vs. 76 ± 28 at d 15, $P < 0.05$ and ΔIsc theophylline, $\mu A/cm^2$: 326 ± 62 at d 0 vs. 125 ± 54 at d 15, $P < 0.05$). In ileum and colon, weaning had no effect on the response to 5-HT or theophylline (data not shown).

Na^+-dependent glucose absorption. In the proximal jejunum, Na^+-dependent glucose absorption was significantly increased on d 2. This increase was transient because glucose absorption had returned to preweaning values by d 5. Moreover, glucose absorption continued to decrease, reaching a level 83% lower on d 15 than on d 0 (**Fig. 2***A*). The pattern of glucose absorption differed in the ileum after weaning. It first declined on d 2 and 5, returned to preweaning values on d 8, and declined again on d 15 (Fig. 2*B*).

Intestinal barrier function

Paracellular permeability. Transmucosal resistance in proximal jejunum dropped on d 2 to a value 68% lower than preweaning values. This effect was transient because R had returned to the preweaning value by d 5 (**Fig. 3***A*). By contrast, ileal transmucosal resistance exhibited a 160% increase on d 5 and remained stable for the rest of the period studied (Fig. 3*B*). Weaning did not alter colonic transmucosal resistance (Fig. 3C).

Permeability to macromolecules. Permeability to macromolecules was assessed by the measure of HRP flux. It dropped transiently in the jejunum on d 2 and 5 postweaning and reached values at d 15 that were not different from those at d 8 but that were lower than the initial preweaning values (**Fig. 4***A*). By contrast, in the ileum and colon, HRP flux was not affected by weaning (Fig. 4*B* and C).

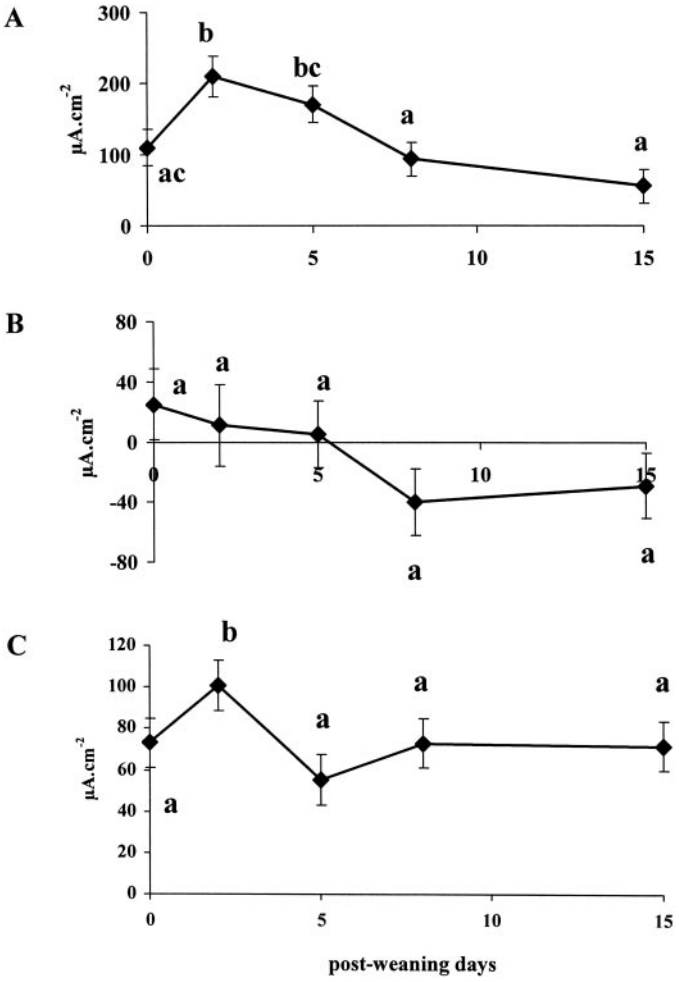

FIGURE 1 Changes in basal short-circuit current (Isc) in the jejunum (*A*), ileum (*B*), and colon (*C*) over time after weaning in piglets. Values are lsmeans ± SEM, $n = 12$. Lsmeans without a common letter differ, $P < 0.05$.

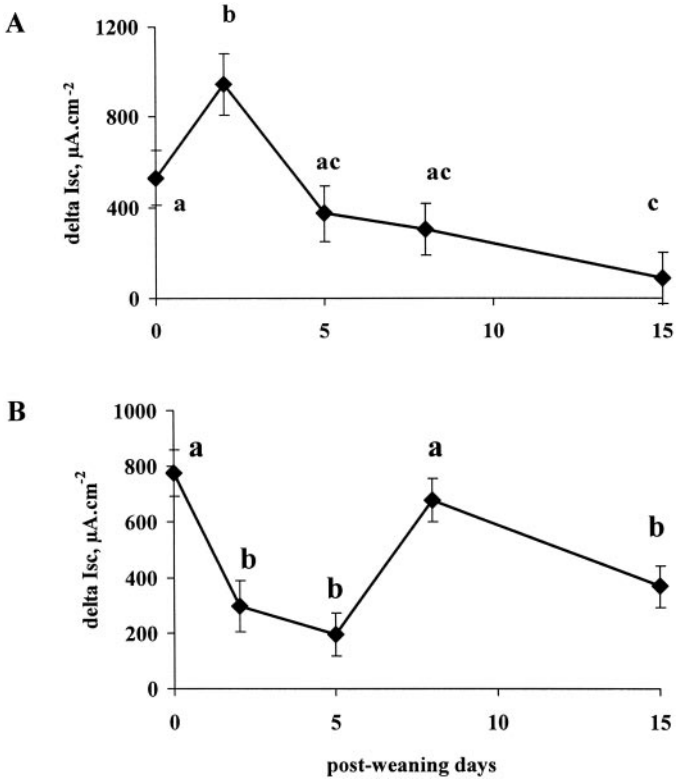

FIGURE 2 Changes in Na^+-dependent glucose absorption in the jejunum (*A*) and ileum (*B*) over time after weaning in piglets. Values are lsmeans ± SEM, $n = 12$. Lsmeans without a common letter differ, $P < 0.05$.

Comparison with older pigs. Proximal jejunum of 9-wk-old standard pigs was studied to assess whether the changes observed 15 d after weaning were long lasting. The comparison of data of d-15 postweaning piglets and older pigs showed that basal Isc and HRP fluxes were lower in older pigs [basal Isc, $\mu A/cm^2$: 56 ± 10 at d 15 vs. −7 ± 7 at d35, $P < 0.05$ and HRP flux, pmol/($cm^2 \cdot h$): 344 ± 57 at d 15 vs. 33 ± 11 at d 35, $P < 0.05$]. By contrast, glucose absorption, response to 5-HT and theophylline, as well as transmucosal resistance, were not different between d 15 and 35 postweaning (data not shown).

DISCUSSION

This study demonstrated that weaning induced dramatic transient as well as long-lasting changes in intestinal physiology, mainly at the small intestinal level. Some of these changes could partly explain postweaning diarrhea. By contrast, they appeared to be independent of the type of diet tested.

The influence of the postweaning diet on the changes observed after weaning seems low because we did not find any significant difference between the 2 groups of pigs for any of the variables studied. The formula of the first diet resembled that of a conventional weaning diet, whereas the second diet was formulated to reach an incorporation level of wheat of 68%. We chose this cereal because it was shown earlier to induce more diarrhea in piglets at weaning compared with barley or corn (12). Wheat-based diets also favor gut disorders in poultry, with altered epithelium-bacteria interactions (13). However, in our case, no negative effects of this diet were observed. The absence of an influence of the type of diet on intestinal disturbances at weaning was also documented for parameters such as villous atrophy or digestive enzyme activity and expression (14), consistent with our results on villous/crypt architecture and lactase and maltase activities. For the architecture of the mucosa, only feeding piglets either sow's or cow's milk at a high level of feed intake was shown to prevent the harmful effect of weaning (15,16). Miller and Skadhauge (17) did not observe any influence of the type of diets used (soy-based or egg-based) on electrolyte transport, emphasizing that the changes observed at weaning might reflect a deep developmental pattern initiated by weaning, one in which the type of diet appears to have little influence.

Weaning was followed by transient changes in intestinal architecture and physiology, i.e., villous atrophy, as already

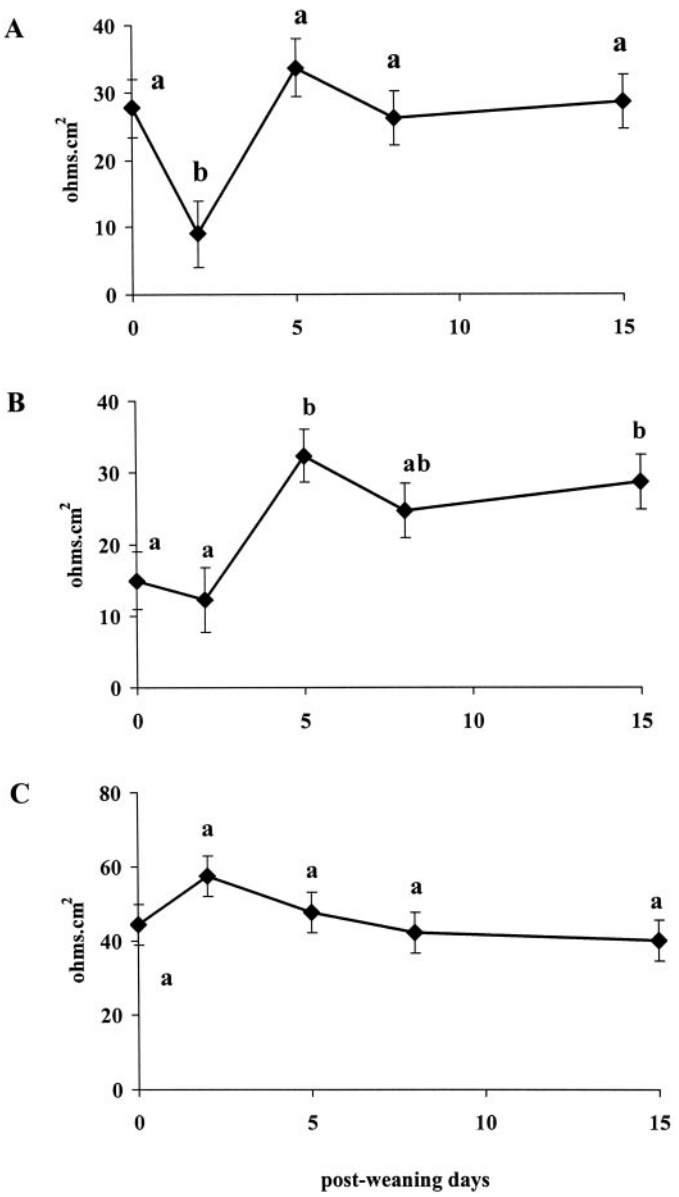

FIGURE 3 Changes in transmucosal resistance in the jejunum (*A*), ileum (*B*), and colon (*C*) over time after weaning in piglets. Values are lsmeans ± SEM, $n = 12$. Lsmeans without a common letter differ, $P < 0.05$.

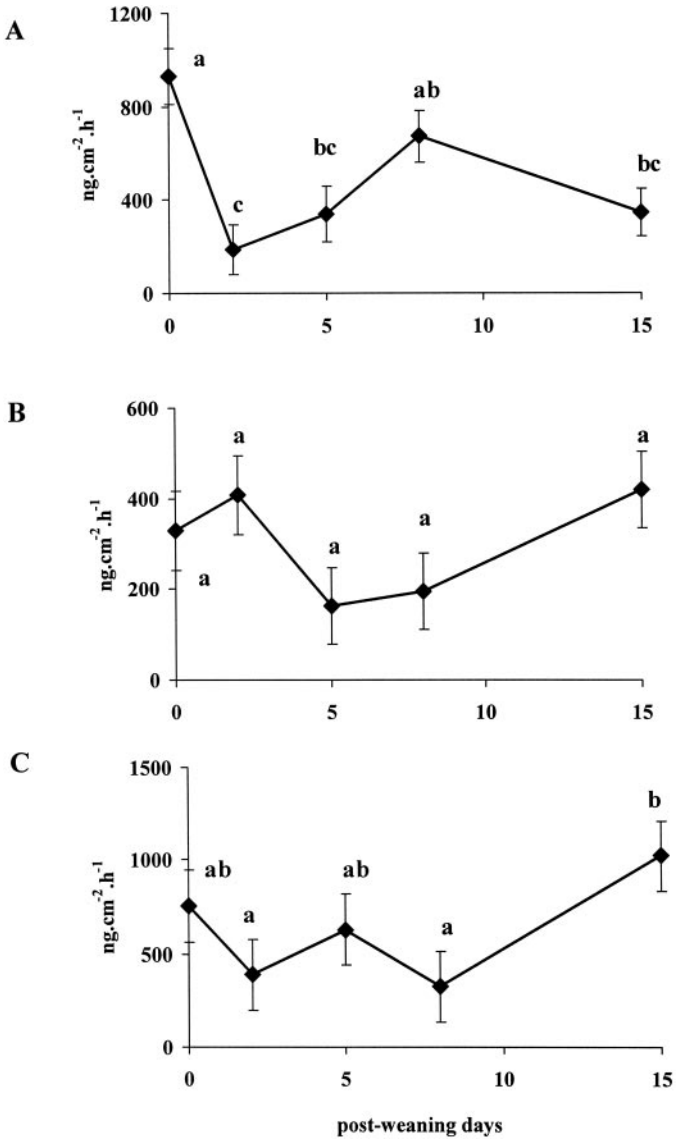

FIGURE 4 Changes in HRP fluxes across the jejunum (*A*), ileum (*B*), and colon (*C*) over time after weaning in piglets. Values are lsmeans ± SEM, $n = 12$. Lsmeans without a common letter differ, $P < 0.05$.

reported in other studies (14), increased jejunal and colonic Isc, and jejunal glucose absorption, decreased ileal glucose absorption and jejunal transmucosal resistance, 2 d after weaning. However, these parameters returned to preweaning values on d 5. Our weaning model combined different stressful events during the first 2 d, i.e., psychological stress with the separation from the mother and mixing with nonlittermates, and nutritional stress because piglets were food deprived for the first 2 d. Both psychological stress and food deprivation dramatically affect intestinal architecture and physiology. The lack of luminal stimulation by nutrients induces villous atrophy (18). Food deprivation in piglets was also shown to decrease transmucosal resistance and to increase short-circuit current, Na^+-dependent glucose absorption and responses to secretory stimuli such as carbachol, histamine, prostaglandins, or 5-HT in the jejunum (19). Similarly, low energy intake at weaning was followed by an increase of permeability to mannitol in the mid intestine of piglets (3). In rats, psychological stress induces an increase in Isc and higher responses to electrical feed stimulation but not to vasoactive intestinal peptide (VIP) or betanechol (20). Psychological stress also increases jejunal permeability to mannitol or ^{51}Cr-EDTA and permeability to macromolecules (20,21). Overall, our data are in agreement with these results, except for the lack of increased responsiveness to secretagogues or permeability to macromolecules. These discrepancies might be due to animal species difference because the effect of psychological stress on gut physiology was studied in rodents, but also to age difference because most of the studies on stress or food deprivation were performed in adult animals.

The changes observed at d 2 were transient, which is in agreement with the effect of fasting, usually also transient. Parameters such as gut atrophy or intestinal permeability are repaired within 3 d of refeeding after a 3-d starvation period in rats (22). Intestinal villous atrophy was also recovered after 4 d of refeeding in underfed piglets weaned at a very early age (23). Similarly, the effect of psychological stress on intestinal function in rats is mainly transient because values for Isc and paracellular permeability of stressed rats did not differ from those of sham-stressed rats 3 and 7 d after the end of a 5-d period of stress (24).

We observed a significant decrease in 5-HT and theophylline-induced secretion in jejunum, of glucose absorption in jejunum and ileum, as well as HRP flux in jejunum and an increase of the transmucosal resistance in ileum on d 15 compared with preweaning values. Basal Isc in ileum also became negative, although the change was not significant. Some of the decreases observed in the jejunum seemed long lasting because the responses to glucose, 5-HT, and theophylline in the older pigs (35 d after weaning) did not differ from those measured on d 15 postweaning. These older pigs were reared in a standard production environment and were not subjected to the same experimental protocol as the other piglets. The comparison, therefore, might not be straightforward. However, the pattern of food intake we chose in the experimental protocol resembles that of piglets at weaning; we can therefore assume that the older piglets also had a transient anorexia at weaning followed by a gradual increase in food intake.

The decrease in basal Isc observed in ileum agrees with observations by Miller and Skadhauge (17) and in our laboratory. Indeed, Miller and Skadhauge observed a decrease in Isc in ileum 7 d after weaning, which could be accounted for mainly by a decrease in net absorption of sodium (17). We also observed negative values for basal Isc in the ileum of adult pigs (unpublished data). Even if our Ussing chamber setup does not allow us to distinguish between Na^+ absorption and Cl^- secretion, we hypothesize that weaning is followed by a decrease in Na^+ absorption in the ileum, resulting in the drop of basal Isc after weaning. Moreover, the decreases in responses to 5-HT, theophylline, or glucose are in accordance with the overall decreased sensitivity to secretagogues, nutrient absorption, and permeability to macromolecules with age in mammals. Indeed, weaning is associated with a decrease in glucose transport activity in rats (25). However, these data were not supported by results obtained with the in vitro everted-sleeve method in pigs, which showed no difference in the rates of transport of glucose between 10-d old piglets and 30-d old piglets weaned at 21 d (5). In examining sensitivity to secretagogues, Skadhauge's group demonstrated in a series of experiments that the responses to 5-HT, VIP, and theophylline decreased between neonates, fully weaned young piglets, and adult pigs (7,8). Because the 5-HT secretory response depends on Ca^{2+} intracellular signaling and not cAMP in porcine

small intestine (8), the decreased response to secretagogues observed in our study seems therefore to reflect a reduced secretory capacity of the tissues with age, irrespective of the intracellular signaling pathway involved. Last, permeability to polyethylene glycol of different molecular sizes also decreased between 36- and 45-h-old and 22- to 28-d-old piglets, indicating a decrease in permeability to macromolecules with age (26).

Taken together, our results suggest that the decreases observed over time (glucose absorption, responses to 5-HT and theophylline, basal Isc in ileum) occur shortly after weaning. Indeed, weaning is regarded as a maturation period for the intestine in a number of animal species, especially in rodents, with the activation of immune cells considered to be a potential mechanism in this maturation phenomenon (27,28). In piglets, weaning is also a key period in terms of maturation of immunity (29). A recent study showed that weaning is followed by transient upregulation of proinflammatory cytokine mRNAs, such as interleukin (IL)-1β, IL-6, and tumor necrosis factor-α (30). Increased T-cell numbers and local expression of the matrix metalloproteinase stromelysin were also reported shortly after weaning (31). Here we demonstrated that as this transient inflammatory process and maturation of the immune system occurs, weaning also induces maturation of the physicological function of the small intestine.

The different segments of the intestine (proximal jejunum, ileum, or colon) had different responses to weaning. In the proximal jejunum, both acute changes and profound maturation modifications occurred, whereas only maturational phenomena were observed in ileum. On the other hand, weaning had little effect on colonic physiology, except for a transient increase of Isc at d 2. Differences between intestinal segments were already noted after weaning. However, these differences were mainly temporal, i.e., villous atrophy was observed very shortly after weaning (1–2 d) in the duodenum or proximal jejunum but occurred in the ileum only a few days later (23). Here, the pattern of modifications was completely different between proximal jejunum and ileum. This was particularly striking for Na^+-dependent glucose absorption patterns, which were completely opposite, resulting in a ratio of Na^+-dependent glucose absorption in ileum to that measured in proximal jejunum varying from 0.3 at d 2 to 4.2 at d 15. The highest Isc response to glucose in ileum at d 15 compared with proximal jejunum agrees with results of Grondahl et al. (32) showing higher electrogenic Na^+ absorption in the mid and distal parts of the small intestine in fully weaned piglets. On the other hand, the opposite absorption capacities in the first days after weaning have never been described. This low absorptive capacity in the ileum could result in an increased risk of osmotic diarrhea. Indeed, the high absorptive capacity in the proximal jejunum at d 2 seems without purpose given the decreased enzymatic activities and villous atrophy observed at the same time. This could result in an enhanced flow of nutrients in the distal part of the small intestine, resulting in osmotic diarrhea due to the low absorptive capacity. In addition, secretory diarrhea could happen at the same time. Indeed, the decrease in jejunal transmucosal resistance and the low transmucosal resistance in ileum observed 2 d postweaning could contribute to an increased access of luminal antigens to the lamina propria, triggering an influx of inflammatory cells and an increase in the level of inflammatory mediators, such as prostaglandins (30,31). Once again, even if our Ussing chambers setup does not allow us to distinguish between Cl^- secretion and Na^+ absorption, we can hypothesize that the increase in Isc at d 2 in proximal jejunum and colon is due to electrolyte secretion induced by the presence of these inflammatory mediators (19,30,31,33). This increase in electrolyte secretion as well as a low reabsorption capacity in the ileum could exceed the reabsorption capacity of the colon and therefore lead to diarrhea.

In conclusion, we demonstrated that weaning induces many changes, both acute and long lasting, in the intestine of piglets. The acute changes are more likely due to the multiple stresses imposed on the piglets at the time of weaning. Reducing these stresses by promoting higher feed intake in the early postweaning period might therefore help to reduce small intestinal structural and functional disorders and diarrhea postweaning.

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