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Lactose Flux Occurs by Differing Mechanisms in the Colon and Jejunum of Newborn Piglets

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ABSTRACT. The unidirectional flux of 10- and 40-mM lactose was studied in newborn porcine jejunum and colon mounted in Ussing chambers. Polyethylene glycol 400 was used to measure passive paracellular permeability. The mucosal-to-serosal flux and the tissue accumulation of labeled lactose from the colon was similar to that of lactose-derived glucose from the jejunum. However, only jejunum showed a lactose-stimulated increase in short-circuit current. In jejunum, glucose was the sole sugar identified in the serosal bath, whereas in colon, only intact lactose was identified. Despite colonic lactose flux, polyethylene glycol oligomers were not found in the serosal bath, suggesting that they do not share the same route of absorption. Colonic lactose transport was nonsaturable between 1 and 40 mM. Under nongradient conditions, no net colonic lactose transport was observed. Cumulatively, these data suggest that the colon, unlike the jejunum, does not contain a glucose-galactose sodium cotransporter. The colon of the newborn piglet transports intact lactose at a flux equal to that of lactose-derived glucose by the small intestine, but by a different mechanism that is as yet undefined. (*Pediatr Res* 33: 568-572, 1993)

Abbreviations

I_{sc}, short-circuit current
PEG, polyethylene glycol
R_t, tissue resistance
TLC, thin-layer chromatography
$J_{m \rightarrow s}$, mucosal-to-serosal lactose flux
$J_{s \rightarrow m}$, serosal-to-mucosal lactose flux

Several studies (1-5) have suggested that the colon of the human neonate, especially the premature infant, may be a major site for the digestion and assimilation of lactose. Estimates of the amount of lactose retrieved from the colon in newborns vary. Based on breath H_2 measurements in human premature infants, estimates by MacLean and Fink (3) suggested that most of the ingested lactose was fermented in the colon. Subsequently, data on the rate of H_2 recovery in the breath of infants after a lactose meal led to a revision of MacLean and Fink's estimates and suggested that the amount of lactose fermented may be 15 to 20% of that ingested (6). Because the daily lactose load is substantial (nearly 13 g/kg/d), the amount passed into the colon could be nutritionally significant. Surprisingly, the newborn neither develops an osmotic diarrhea nor loses excessive amounts of carbohydrate in the stool (2, 4, 5). Based on the available data, researchers have inferred that, as in adults, bacterial fermentation is the primary mechanism whereby the newborn salvages lactose energy that would otherwise be lost (7).

However, it has been shown that even when colonic bacterial population is low, the newborn can still recover lactose from the lumen of the colon. *In vivo* colonic perfusions in newborn piglets, in which the bacteria had been depleted by flushing with normal saline, demonstrated that the colonic mucosa absorbs the lactose at a rate up to 20-fold greater than it absorbed an equimolar mixture of glucose and galactose, the monosaccharide constituents of lactose (8). This phenomenon was not the result of prior action of bacterial or colonic mucosal β-galactosidase activity; both were shown to be negligible.

In the current study, lactose uptake was compared in the jejunum and the right colon of the newborn piglet using tissues mounted in Ussing-type chambers. $J_{m \rightarrow s}$ and appearance of carbohydrate in the serosal bath were determined, and measurements of the I_{sc} and R_t were made. Saturability of lactose absorption using mucosa-to-serosa gradients between 1- and 40-mM concentrations and the absorption of lactose under nongradient conditions were tested. PEG 400, a mixture of homologous oligomers that are insoluble in lipids, was used to determine whether diffusion through paracellular channels was enhanced by the presence of lactose (9, 10).

MATERIALS AND METHODS

Animal and Tissue Preparation. All studies were approved by the Animal Care and Use Committee. Newborn Yorkshire piglets (3 to 4 d old; 1.8 to 2.6 kg) were obtained from the swineherdsman and delivered to the lab on the morning of the study. The piglets had been exclusively fed sow milk. Piglets were anesthetized with pentobarbital (35 mg/kg intraperitoneally) within 1 h after procurement. A midline incision was made, and the entire small and large bowel was excised. The excised gut was immersed in iced Ringer's solution containing (in mmol/L): Na^+, 136; K^+, 6; Cl^-, 130; HCO_3^-, 14; H_2PO_4, 1.2; Ca^{++}, 2.5; Mg^{++}, 1.2; pH 7.4, that had been bubbled with 95% O_2:5% CO_2. Transport of the tissue to the laboratory took 1 min. The animal was euthanized by i.v. injection of concentrated pentobarbitol. Twenty-cm segments of jejunum beginning 10 cm distal to the ligament of Treitz, or of right colon beginning just distal to the ileocecal valve, were opened along the antimesenteric border, stripped of serosa and longitudinal muscle, and mounted in standard Ussing-type chambers (1.12-cm^2 surface area) within 20 min of anesthesia. The water-jacketed apparatus was bathed at 40°C by a circulating water bath (model 2161, Forma Scientific, Marietta, OH). The mucosal and serosal sides were individually bathed in Ringer's solution oxygenated with 95% O_2:5% CO_2 via a glass

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bubble-lift apparatus (World Precision Instruments, Sarasota, FL).

Study 1: Transepithelial Lactose Flux from Colon and Jejunum. Four jejunal and four colonic tissues from each of five piglets were mounted under short-circuited conditions using a four-electrode automatic voltage clamp, capable of measuring transepithelial potential difference and automatically subtracting fluid resistance (DVC 1000, World Precision Instruments). Tissues were allowed to equilibrate for 30 min before cold and [$U^{14}C$]lactose were added to the mucosal bath (11). To maintain transepithelial isotonicity, an equal amount (mol) of mannitol was added to the serosal bath. The added lactose was sufficient to achieve a final concentration of either 10 mM or 40 mM in separate tissues and corresponding sp act of 0.02 μCi/mmol and 0.005 μCi/mmol. Thus, although there was not an osmotic gradient between mucosal and serosal compartments, there was a lactose concentration gradient. The final mucosal and serosal osmolality was adjusted to 360 mosmol with mannitol; this value is representative of the osmolality in the colon during the first week of life (12). The transport study was allowed to proceed for 60 min.

The following assays were performed and are described in detail below. R_t and I_{sc} were measured. Flux of lactose was calculated from measured dpm in the serosal bath. The amount of serosal lactose, glucose, and galactose was determined by TLC and colorimetry. Tissue accumulation of ^{14}C was determined by scintillation counting of solubilized specimens of exposed tissues.

Study 2: Saturability of Lactose Absorption. To assess the saturability of the lactose transport mechanism, the same conditions as those in study 1 were repeated using six concentrations of lactose in the mucosal bath of mounted colonic tissues: 1, 5, 10, 20, 30, and 40 mM. A 10-mM (4 g/L) solution of PEG 400 (molecular mass 150–590 D; the value of 10 mM was based on the average molecular mass of 400 D) was added to the mucosal bath as a marker of paracellular permeability. Osmolality was balanced in the serosal bath with mannitol. Flux of lactose was determined as in study 1. To measure PEG movement, the serosal fluid was analyzed for individual oligomers and the flux (in $nmol \cdot cm^{-2} \cdot h^{-1}$) calculated, as detailed below.

Study 3: Absorption of Lactose under Nongradient Conditions. Lactose flux in studies 1 and 2 occurred under gradient conditions for the sugar. To examine the possibility that the transport process was active, in this experiment, the lactose gradient was abolished. Matched colonic tissue pairs, differing in resistance by no more than 25%, were used to measure unidirectional flux ($J_{m \to s}$ and $J_{s \to m}$) with [^{14}C]lactose (0.02 μCi/mmol) added to either the mucosal or serosal test bath. Net flux was determined by subtracting $J_{s \to m}$ from $J_{m \to s}$.

Assays. Tissue viability. Tissues were deemed viable if the R_t remained unchanged during the study, if theophylline caused an immediate increase in I_{sc} when added to the circulating bath at the end of the study, and if the PEG 400 and carbohydrates present did not equilibrate with the concentrations in the contralateral bath.

Electrophysiologic measurements. R_t and I_{sc} were calculated as previously detailed (11). Data from each chamber were graphically recorded (Linear Instruments, Houston, TX); the data from all eight chambers were simultaneously collected and stored using an IBM PC-XT computer with analog to digital converters.

Flux measurements. The tissue was equilibrated in buffer for 30 min. After labeled and unlabeled lactose were added to the bath, a 5-min circulation period was allowed before a 0.5-mL baseline (0 time) aliquot was withdrawn from both baths. One sample (0.5-mL) was stored for later analysis in 50 μL of 2 N NaOH to prevent bacterial digestion (13). After 60 min, another 0.5-mL sample was withdrawn from each bath and treated in the same manner. Another set of 0- and 60-min samples were immediately processed for scintillation counting (Tri-Carb 2200 CA, Packard Instruments, Downers Grove, IL) to assess tissue integrity. Samples that showed equilibration between mucosal and serosal dpm of ^3H or ^{14}C were deemed punctured, and the data from that tissue were discarded.

To measure the flux of lactose, the entire serosal solution was drained into a tared vial containing 1 mL of 2 N NaOH. The solution was weighed, desalted over a 1 × 20 cm column of Amberlite MB3 (a mixed cationic/anionic resin) that was washed with 7 to 10 volumes of deionized water. The effluent was lyophilized to dryness and reconstituted in 1 mL of distilled water. The results from scintillation counting were used to calculate flux using standard calculations (11).

Carbohydrate assays. After incubation, aliquots of mucosal fluid (10 μL) were removed to quantitate mucosal accumulation of glucose and galactose, formed by the enzymatic hydrolysis of lactose; they were assayed by TLC (LK5D silica gel plates, Whatman, Clifton, NJ), as described in previous reports (11, 13, 14). The plates were developed with butanol:acetone:water (5:4:1 vol/vol) and stained with an anisaldehyde reagent (15). This stain detects as little as 1 μg (5.5 nmol) of glucose without interference from mannitol.

To quantitate the concentrations of the three carbohydrates in the serosal bath, the following procedure was used. After the entire serosal bath was lyophilized to dryness and reconstituted in water twice, a 50–100× concentration of the serosal bath solution was achieved. A 10-μL aliquot was analyzed by the phenol sulfuric acid colorimetric method for total carbohydrate concentration (16). A second 10-μL sample was applied to a TLC plate; the adjacent lane contained lactose, glucose, and galactose standards. The plate was developed and dried. The sites of the individual carbohydrates were identified on the lanes with standards, and the sites were marked on the remaining (unstained) lanes. The silica gel within each identified area was scraped into a test tube and subjected to the phenol sulfuric acid assay. In this way, the quantity and ratio of the three test carbohydrates and the total carbohydrate in the serosal bath was calculated. Although the TLC method could visualize a spot containing as little as 5.5 nmol (1 μg) of glucose on the silica gel, the phenol sulfuric acid method of analyzing silica gel spots was not accurate below 20 nmol (4 μg) glucose. Because the serosal bath was completely recovered and concentrated 50- to 100-fold, the sensitivity of the TLC/phenol sulfuric acid assay was deemed ample for the quantification of carbohydrate in these studies.

Tissue accumulation of ^{14}C or ^3H. The portion of the mounted jejunal and colonic tissue that was exposed to the incubation baths was carefully excised from the lucite chambers and blotted on filter paper. After weighing, a portion was removed for protein analysis. The tissue was solubilized (Soluene 350, Packard) overnight in a 60°C water bath and the dpm were quantified with Hionic-Fluor (Packard), with the aid of a program for dual-label analysis of ^3H and ^{14}C. Counts were normalized per mg of tissue protein, using a modification of the Bradford method (17).

PEG profile. PEG movement was assayed in study 2 to determine whether varying concentrations of lactose from 1 to 40 mM could stimulate paracellular diffusion. A 0.5-mL aliquot of the serosal bath was removed and lyophilyzed (10× concentration) for analysis of the PEG flux, as previously described (18, 19). After desalting, HPLC (HP 1050 with an HP 1047 refractive index detector, Hewlett-Packard, Palo Alto, CA; Waters C18 column, Milford, MA; eluant: methanol:H_2O 1:3, vol/vol) was used to separate and quantify the eight individual serosal PEG oligomers in relation to a standard curve generated by a set of external standards. To identify at least five of the PEG oligomers, a serosal bath concentration of 5 nmol/mL of PEG was necessary; this represents a lower limit of detection for PEG flux of 45 $nmol \cdot cm^{-2} \cdot h^{-1}$. When the serosal bath sample was lyophilized, the lower limit of detection for PEG flux was 0.45 $nmol \cdot cm^{-2} \cdot h^{-1}$. The lactose flux was determined in the same 0.5-mL sample to compare with the PEG flux.

Materials. Lactose, glucose, galactose, and mannitol were obtained from Sigma Chemical Co., St. Louis, MO. PEG 400 was purchased from Fisher Scientific, Fairlawn, NJ. The [U-^{14}C]

lactose was purchased from New England Nuclear Dow Research Products, Boston, MA. Amberlite MB3, a mixed-bed resin, is a product of Mallinckrodt, Paris, KY.

Statistics. Results are expressed as means ± SEM. Statistical analysis was performed using both paired and unpaired t test where appropriate. A one-way analysis of variance was used to compare lactose flux with lactose concentration. Linear regression of the log values was also used to confirm that lactose flux was a linear function with respect to lactose concentration; p values <0.05 were considered significant.

RESULTS

Study 1: Flux of Lactose in Jejunum and Colon. Flux of lactose. The unidirectional flux of lactose in the jejunum and in the colon is presented in Table 1. The magnitude of colonic $J_{m\to s}$ in the presence of 10 mM lactose (500 ± 100 $nmol \cdot cm^{-2} \cdot h^{-1}$) and in the presence of 40 mM lactose (1431 ± 190 $nmol \cdot cm^{-2} \cdot h^{-1}$) was similar to that of lactose-derived glucose observed in the jejunum (560 ± 80 and 1710 ± 260 $nmol \cdot cm^{-2} \cdot h^{-1}$ in the presence of 10 and 40 mM, respectively).

Tissue accumulation. Although accumulation of counts was substantial, no tissue contained more than 5% of the original ^{14}C that had been placed in the mucosal bath (maximum, 18.5 nmol lactose/mg protein). There was no further accumulation of ^{14}C in jejunal and colonic tissues exposed to 40 mM when compared with those exposed to 10 mM lactose.

Electrophysiologic data. Despite similarities in $J_{m\to s}$ and in tissue retention of lactose between the two intestinal segments, only the jejunum showed a significant increase in I_{sc} in the presence of mucosal lactose (11 ± 1.6 and 25 ± 5.7 $\mu A \cdot cm^{-2}$ for 10 and 40 mM, respectively). The values for I_{sc} were similar to those reported by other investigators (20) using newborn suckled piglet ileum.

Carbohydrate analysis. Analysis of the serosal solution for carbohydrates indicates a difference in the fate of lactose incubated with jejunal or colonic tissues. Figure 1*A* and *B* shows the accumulated carbohydrate species on both serosal and mucosal baths surrounding the jejunal and colonic tissues after 60 min of mucosal exposure to 10 mM lactose. In the serosal (contralateral) bath of the jejunal specimens, the carbohydrate identified was glucose (Fig. 1*A*). By contrast, in the serosal baths of the colonic specimens, intact lactose accounted for over 95% of the transported carbohydrate. Galactose was not identified on any of the TLC plates. Analysis of the mucosal samples showed that, when jejunal tissue was exposed to lactose, glucose and galactose accumulated on the mucosal side; when colonic tissues were exposed to lactose, monosaccharides did not accumulate on the mucosal side (Fig. 1*B*).

Study 2: Saturability of Lactose Absorption. Flux data. The flux of lactose did not show saturation up to a concentration of 40 mM (Fig. 2). By one-way analysis of variance, the lactose flux was a function of lactose concentration ($p < 0.001$). A linear relationship between the log of flux and concentration was seen

Table 1. *Unidirectional carbohydrate flux from 10- and 40-mM mucosal lactose solutions under voltage clamped conditions in isolated newborn porcine jejunum and colon**

	n	I_{sc}	R_t	$J_{m\to s}$
Jejunum				
10 mM	10	11 ± 1.6	35.7 ± 5.7	560 ± 80
40 mM	10	25 ± 5.7	37.8 ± 5.7	1710 ± 260
Colon				
10 mM	10	3 ± 2.1	60.6 ± 7.2	500 ± 100
40 mM	10	−2 ± 2.7	54.8 ± 2.7	1431 ± 190

* Values are means ± SEM of five animals; n = no. of tissues. I_{sc} ($\mu A \cdot cm^{-2}$) represents the difference between baseline (steady state) and maximal stimulation after the addition of lactose to the mucosal bath. $J_{m\to s}$ is reported in $nmol \cdot h^{-1} \cdot cm^{-2}$; R_t is reported in $ohm \cdot cm^2$.

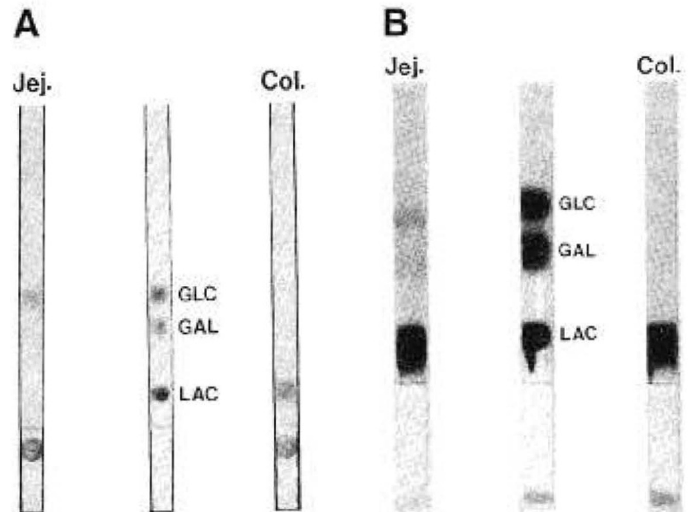

Fig. 1. Representative TLC showing the carbohydrates that accumulated in the serosal bath during studies in which lactose (10 mM) was incubated in the mucosal bath. After a 60-min incubation, the serosal bath was collected, lyophilized, and reconstituted in water (approximately a 50× concentration); a 10-μL sample was applied to the diatomaceous preabsorbant area of the silica gel thin-layer plates. After separation by solvent, the carbohydrates, glucose (*GLC*), galactose (*GAL*), and lactose (*LAC*), were stained with an anisaldehyde reagent. The presence of as little as 1 μg (5.5 nmol) of glucose can be visually appreciated by this method. *A*, serosal samples after 60-min incubations with jejunum and with colon. The *center lane* contains the control carbohydrates for reference. *B*, mucosal samples collected after incubation, showing the effects of mucosal enzyme activity on lactose in the jejunal but not the colonic tissues.

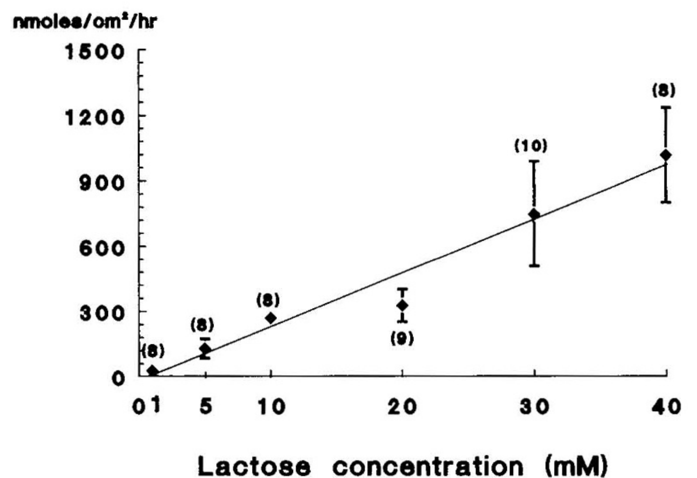

Fig. 2. The relationship between increasing lactose concentration and lactose flux. All values represent mean ± SEM from eight or more tissues (*number in parentheses*) obtained from three or more 4-d-old piglets. The flux of lactose was related to the lactose concentration ($p < 0.001$), and their relationship was linear (r = 0.944) within the concentration range tested.

(r = 0.944), with no indication of an asymptote to suggest saturation within the range of concentrations tested (not shown).

PEG profile. Movement of PEG 400 oligomers across the mucosa to the serosal bath was not detected, despite a 1-h incubation. The lower limit of detection for PEG flux, using the HPLC methodology, was 45 $nmol \cdot cm^{-2} \cdot h^{-1}$. A 10-fold concentration of the serosal bath also did not reveal any PEG peaks; therefore, the flux of PEG (<0.45 $nmol \cdot cm^{-2} \cdot h^{-1}$) was at least 1000-fold less than the flux of lactose (a mean of 500 $nmol \cdot cm^{-2} \cdot h^{-1}$).

Study 3: Absorption of Lactose under Nongradient Conditions. Comparisons between the jejunum and colon are presented for $J_{m \to s}$, $J_{s \to m}$, and net flux in Table 2. As expected, an appreciable net flux (680 $nmol \cdot cm^{-2} \cdot h^{-1}$) of lactose-derived glucose remained across the jejunal tissues despite the elimination of the gradient for lactose, whereas net lactose flux across the colonic tissues was completely abolished when the lactose gradient was absent. Differences in the net lactose flux between the jejunal and colonic tissues were significant ($p < 0.01$).

DISCUSSION

Cumulatively, the results of these studies demonstrate that the colon of the newborn pig can transport intact lactose from the mucosal to the serosal bath by a mechanism that does not require enzymatic cleavage of lactose, generate an I_{sc}, or appear to be carrier-mediated and yet does not appear to occur by a process of nonselective paracellular diffusion.

In a previous study, we used *in vivo* perfusions in piglets up to 25 d of age to demonstrate that lactose was absorbed from the colon 20 times faster than glucose and galactose from a solution that was equimolar in terms of hexose moieties (8). The mechanism of lactose absorption from the colon did not appear to involve β-galactosidase activity or fermentation. The *in vitro* study reported in this manuscript extends our previous findings. The data confirmed that lactose absorption occurred from the colon when measured directly as serosal appearance (flux) rather than indirectly as disappearance from the colonic lumen. The results further demonstrated that the transported species was the disaccharide, lactose, and not cleavage products (glucose and galactose) or fermentation products (short-chain fatty acids). The restricted movement of PEG 400, a well-characterized marker for passive colonic permeability, and of glucose and galactose, supported the idea that the uptake of lactose was a selective process.

The mechanism responsible for transport of intact lactose across the colon in newborns could involve a membrane transport carrier different from that of the small intestine; paracellular movement (*i.e.* by mass transport); transcellular transport (*i.e.* by endocytosis); or some other, as yet undefined, process. Active transport processes, such as the glucose carrier in the small intestine, demonstrate saturability, energy dependence, and net flux against a concentration gradient. Potter *et al.* (21) reported glucose transport during colonic perfusion in rats immediately after birth. Similarly, Henin and Smith (22) showed that neonatal piglet colon is capable of phlorizin-sensitive electrogenic transport of glucose in the first hours of life, a process analogous to that seen in the jejunum; however, the mechanism disappeared by the second day of life. In our study on 4-d-old piglets, colonic lactose transport was not saturable and did not result in net movement when the concentration gradient was abolished. Therefore, carrier-mediated active transport is unlikely. Simple diffusion, which would favor transport of smaller molecular weight substances, is also unlikely. Although lactose (molecular mass 342 D) was transported in colon, smaller oligomers such as glucose (molecular mass 180 D) and PEG oligomers (molecular mass <342 D) were not found in the serosal bath, suggesting that indiscriminant paracellular movement did not occur.

Table 2. *Net carbohydrate flux from 10-mM lactose solution under nongradient conditions in isolated newborn porcine jejunum and colon**

	n	$J_{m \to s}$	$J_{s \to m}$	J_{net}
Jejunum	29	869 ± 89	396 ± 60	608 ± 91
Colon	25	246 ± 47	275 ± 32	−30 ± 22

* Values are means ± SEM from eight animals; n = no. of tissues. J_{net}, the difference between $J_{m \to s}$ and $J_{s \to m}$. $J_{m \to s}$, $J_{s \to m}$, and J_{net} are reported in $nmol \cdot h^{-1} \cdot cm^{-2}$. Differences in the J_{net} between the jejunal and colonic tissues were significant ($p < 0.008$).

Passive movement of intact disaccharide could be postulated to occur through the tight junctions between the colonocytes. A model for the paracellular transport has been proposed for the small intestine, suggesting that the bulk of luminal glucose and amino acids is absorbed by passage through the tight junctions (23, 24). This process is believed to be initiated by the active transport of glucose which, by creating an osmotic gradient between the intercellular space and the intestinal lumen, stimulates contraction of the cytoskeletal proteins and opening of the intercellular tight junctions. The open channel allows hydrophilic nutrients to pass between the cells in association with water flow. In their studies, Pappenheimer and Reiss (25) used passively absorbed markers, including creatinine (molecular mass 113 D), PEG (molecular mass 4000 D), phenolsulfonphthalein (molecular mass 342 D), and inulin (molecular mass 5500 D), to demonstrate a nonselective paracellular movement associated with fluid absorption. These investigators used an *in vivo* perfusion model with glucose (25 mM) as the actively transported species.

To test the hypothesis that paracellular diffusion accounts for passage of lactose across the colonic mucosa, we included PEG 400, a mixture of nonmetabolizable ethylene glycol oligomers with a molecular mass range of 150 to 590 D. PEG 400 permeation of the colonic mucosa has been shown to be mediated almost exclusively by paracellular diffusion (26). The molecular masses of the oligomers in PEG 400 span those of glucose and galactose (molecular mass 180 D) and lactose (molecular mass 342 D). In our studies, the flux of the disaccharide was tested between 1 and 40 mM, values that represent the range of physiologic luminal concentrations, to test the putative opening of intercellular channels (23, 27). PEG was not found in the serosal bath even when the bath was concentrated 10-fold; nonetheless, the disaccharide passed into the serosal bath at a rate equal to that of lactose-derived glucose in the jejunum. Therefore, on a molar basis, PEG passage was at least 1000-fold less than the movement of lactose. These findings suggest that nonselective sieve-like intercellular movement is not likely to be the explanation for lactose transport in our studies.

An alternative transport route, transcellular endocytosis, could account for the appearance of intact lactose. Evidence exists for an active endocytic process in the principle cells of the colon in the newborn rat. Ono (28) has shown by electron microscopy that a tubulovesicular network with lysosomal granules is present in the first days of life but disappears by the end of the first week. Molecules as large as horseradish peroxidase (molecular mass 160 000 D) were transported by this network in the colon of the 4- to 5-d-old rat (29). In piglets and in human neonates, a similar intracellular transport system can be found in the small intestine and colon in the late fetal and immediate neonatal period (30, 31). More definitive studies on endocytosis as a means of lactose transport are not feasible on mounted tissues in the Ussing chamber.

Our TLC data from the jejunal controls are somewhat surprising. In the serosal bath of the jejunum, lactose-derived glucose was the sole species identified. The absence of galactose suggests that after the digestion of lactose occurs at the small-bowel mucosal surface, galactose undergoes another metabolic step: either further digestion, utilization, or epimerization to glucose. Studies in human newborns ingesting lactose have shown that galactose is present in blood in much lower amounts than glucose after a lactose meal, a finding that has been attributed to avid first-pass clearance through the liver (32). Metabolism of galactose or its epimerization to glucose before exit from the enterocyte might be alternative explanations for low-serum galactose levels under such conditions.

In summary, these studies provide evidence for a functional lactose transport process in the colon of the newborn pig. The rate of transport is significant—equal to that of lactose-derived glucose in the jejunum. However, the mechanism of colonic transport of lactose appears distinct from that in the small

intestine. Under physiologic conditions, *i.e.* in the presence of a normal colonic bacterial flora, such a transport system may not be extensively utilized. But when the bacterial flora are depleted, such as occurs during diarrhea, after antibiotics, or in the first days of life, such a transport process may enable the newborn to salvage lactose that escapes assimilation in the small intestine and prevent a potentially lethal osmotic diarrhea (33).

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