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Lactose Assimilation by Full-Term Infants: Relation of [^{13}C] and H_2 Breath Tests with Fecal [^{13}C]Excretion

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Summary

Colonic salvage of malabsorbed carbohydrate is probably a quantitatively important mechanism of lactose assimilation in the premature infant. The relative roles of the small and large intestines in carbohydrate absorption have not been assessed in the full-term infant. The [^{13}C]-1-lactose (^{13}C-1-L) breath test was first validated against [^{14}C]-1-lactose (^{14}C-1-L) in seven adult volunteers. Individual coefficients of correlation of the regression of % dose [^{13}C] (% d [^{13}C]) on % dose [^{14}C] (% d [^{14}C]) for the seven adults varied from 0.950–0.997; the ratio of the cumulative % dose [^{13}C] (cum % [^{13}C]) to the cumulative % dose [^{14}C] (cum % [^{14}C]) ranged from 0.89–1.15. Nineteen full-term infants (40.1 ± 0.9 wk gestation) were subsequently studied. On day 1 baseline breath and stool collections were carried out with unlabeled substrate (lactose-containing formula). In the initial ten infants [^{13}C]-1-L was added to the 7 a.m. or 8 a.m. formula feeding on day 2 and an 8-h breath test was done. A 24-h stool collection was also carried out. In nine subsequent infants a breath test and stool collection with [^{13}C]-1-glucose ([^{13}C]-1-G) were carried out on day 2 and the studies with [^{13}C]-1-L were moved to day 3. H_2 and % d [^{13}C]/h and cum % [^{13}C] in breath and [^{13}C] recovered in stool were determined.

All infants had detectable H_2 in breath on the days of study. Peak H_2 excretion was <20 ppm in eleven infants. ≥20 ppm in eight. There was no relationship of H_2 excretion to gestational age, birth weight, postnatal age or lactose intake. In all 19 infants the % d [^{13}C] in breath per h and the cum % [^{13}C] after [^{13}C]-1-L were virtually identical to data in adults studies after consumption of naturally [^{13}C]-labeled maize glucose. In the infants studied with both substrates, there were no significant differences between [^{13}C]-1-L and [^{13}C]-1-G in % d [^{13}C] at each time point. Cum % [^{13}C] recovered from [^{13}C]-1-G become progressively greater than that from [^{13}C]-1-L, significantly so at 6, 7, and 8 h (8 hour % d [^{13}C]: lactose, 32.6 ± 3.5% and glucose, 35.5 ± 3.1%; paired t = 2.528, $P < 0.05$).

Excess [^{13}C] (1.9% of dose) was detected in the stool of only one infant in the 24 h after [^{13}C]-1-G ingestion. Fecal [^{13}C] after [^{13}C]-1-L was 1.6% of the dose in nine infants (range 1.6–6.8%).

Breath and stool data from these studies imply that lactose absorption in the small intestine by the formula-fed full-term infant is nearly complete. Colonic salvage of carbohydrate occurs but is variable and appears to be quantitatively less important than is suspected in premature infants.

Abbreviations

[^{13}C]-G, [^{13}C]-glucose
[^{13}C]-1-G, [^{13}C]-1-glucose
[^{13}C]-L, [^{13}C]-lactose
[^{13}C]-1-L, [^{13}C]-1-lactose
[^{14}C]-1-L, [^{14}C]-1-lactose
cum, cumulative
d, dose

Neutral β-galactosidase (lactase) located in the bush border of the small intestinal enterocyte is the enzyme responsible for the hydrolysis of lactose, which is the rate limiting step in lactose absorption (8, 11). Lactase, unlike sucrase and maltase, remains low in concentration during fetal development until approximately 36 wk of gestation and then increases continuously thereafter until term (1, 10). Normal full-term infants, whose only natural dietary carbohydrate is lactose, have always been considered "by definition" to be lactose tolerant. Implicit in this belief have been the concepts that intestinal lactase is wholly responsible for lactose digestion and that the entire process of digestion and absorption takes place in the small intestine.

Auricchio and his collaborators (2) were among the first to question these concepts. Based on *in vitro* studies with material obtained at autopsy they concluded that the "large lactose load of the breast-fed (full-term) infant probably exceeds the ability of the small intestine to hydrolyze this sugar" (2). Both the low pH of stool and the finding of significant (≥1%) amounts of reducing substance in the stool of healthy term infants corroborate this idea and suggest that carbohydrate normally passes beyond the ileocecal valve. The excretion of hydrogen in breath in substantial amounts implicates the colonic microflora in anaerobic fermentation of this malabsorbed carbohydrate (3, 6). In addition to hydrogen gas, volatile fatty acids are produced. These compounds have been shown to be absorbed in the colon of the adult (15).

The colonic salvage of carbohydrate malabsorbed in the small intestine is probably a quantitatively important mechanism of lactose assimilation in the premature infant who is born with low intestinal lactase (14). The relative roles of the small and large intestines in carbohydrate absorption have not been assessed in the full-term infant.

Hydrogen production requires a fecal flora capable of fermenting the malabsorbed carbohydrate. Low breath hydrogen could be interpreted to mean complete absorption in the small intestine but is equally compatible with the lack of a fully developed fecal flora, especially in the infant studied shortly after birth. The availability of a stable isotopically labeled [^{13}C]-L molecule presented the opportunity to use a tracer to study lactose assimilation

in infants, by estimating the amount that was absorbed from the appearance of excess [$^{13}CO_2$] in breath, as well as the amount that was excreted in stool, by estimating the excess [^{13}C] content of stool. These data were related to data on breath hydrogen excretion collected as part of the same study.

MATERIALS AND METHODS

Validation of [^{13}C]-L breath test against [^{14}C]-L. Seven adult volunteers were studied after an overnight fast using an aqueous solution of 50 g of lactose containing 1 g of [^{13}C]-1-L (43 atom percent excess, APE) (Merck, Sharp & Dohme, Ltd., Montreal, Canada) and 5 μC of [^{14}C]-1-L (Amersham, Arlington Heights, IL). Breath samples were collected 0.5 and 0.25 h before administration and at 0.5, 1, 2, 3, 4, and 5 h thereafter. Expired carbon dioxide was trapped quantitatively in base and [$^{14}CO_2$] in expired air was determined by liquid scintillation counting. Breath samples were also placed in 50 ml Vacutainers and the [$^{13}CO_2$] excretion was later determined by isotope ratio analysis using previously described methods (19). The % dose excreted per h at each time point and the 5-h cum % d recovered (area under the curve) for the two isotopes were compared.

Subjects. Nineteen full-term infants (40.1 ± 0.9 wk gestation) were studied after uncomplicated elective Caesarean section infants born by vaginal delivery are discharged at 3 days of age and consequently their inclusion in the study would have required prolonging their hospitalization for the 3- or 4-day protocol). Birth weights averaged 3.35 ± 0.44 (S.D.) kg. Infants entered the study at 4.6 ± 0.5 days of age. The mothers of all infants had elected not to breastfeed their infants. Intakes of formula (29) on the initial day of the study were 98 ± 14 Kcal/kg body weight/day (15 ± 3 Kcal/kg body weight/feeding, 1.5 ± 0.3 g lactose/kg/feeding) and were essentially the same on subsequent days.

Protocol. During the first day of each study a 24-h stool collection with unlabeled substrate (lactose-containing formula) was carried out. In the initial ten infants, [^{13}C]-1-L (43 APE, 475 mg/m^2) was added to the 7 a.m. or 8 a.m. feeding on day 2 of the study. End expiratory breath samples were collected in duplicate 0.25 and 0.1 h before the feeding and then at 0.5, 1 h, and subsequent hourly intervals thereafter to 8 h after the test meal through a small feeding tube placed just inside one nostril, as in previous studies (4, 9). The first three infants studied were sampled only for a period of 5 h. After initial analysis of their breath curves indicated that further time points would yield additional information, the studies were extended to 8 h). Infants were fed on schedule 4 h after the test feeding but additional [^{13}C[-1-L was not added to this feeding. Breath samples for H_2 determination were analyzed within several hours of collection. Samples for [$^{13}CO_2$]/[$^{13}CO_2$] isotope ratio analysis were transferred to 50 ml Vacutainers for storage, shipment, and subsequent analysis. All stools passed on day 1 and on the subsequent two days were collected on diapers lined with polyethylene wrap. Immediately after collection each stool was placed into a tared container for that day's collection, to which $HgCl_2$ had been added to stop further bacterial fermentation, and frozen.

After the first ten infants had been studied it became clear that the addition of a study with [^{13}C]-1-G in each infant was desirable. This would serve to control for differing rates of intestinal absorption of glucose and of glucose metabolism among infants. Because glucose absorption was expected to be essentially complete with little label excreted in the stool, all studies with [^{13}C]-1-G were carried out on the day before the studies with [^{13}C]-1-L (baseline breath excretions of [$^{13}CO_2$] return to normal within 24 h after the test does with either substrate). In the modified protocol, a breath test with [^{13}C]-1-G (90 APE) (Merck, Sharp and Dohme, Ltd., Montreal, Canada) and a 24-h stool collection were carried out on day 2; a breath test with [^{13}C]-1-L and a 24-h stool collection were carried out on day 3; and a final 24-h stool collection was obtained on day 4. A dose of 120 mg/m^2 of [^{13}C]-1-G was used to provide the same amount of excess [^{13}C] provided by [^{13}C]-1-L and was added to the 7 a.m. or 8 a.m. feeding.

Laboratory methods. Breath H_2 was determined in duplicate on a Quintron (Milwaukee, WI) Model S gas chromatograph modified as suggested by Solomons *et al.* (21) using argon as a carrier gas (accuracy ± 4 ppm). The instrument was calibrated against a standard of 52.5 ppm H_2 in room air. Breath CO_2 was isotopically analyzed on a dual inlet automated Nuclide 3–60 mass spectrometer, as previously described (19).

After thawing, each 24-h stool collection was adjusted to pH 9 and homogenized with three times its weight in water. Six to ten milliliters of the homogenate were placed in a seamless regenerated cellulose dialysis bag and dialyzed against three 700 ml volumes of distilled water over a period of 24 h. Previous studies with [^{14}C]-G had shown this precedure to effect complete dialysis of water-soluble carbohydrate; consequently, no internal standard was used. Both the homogenized stool and the non-dialyzable fraction were submitted for isotopic analysis. Combustion of stool samples, isolation, and purification of the resulting CO_2 and [^{13}C]/[^{12}C] analysis were carried out as in previous studies (18). The determinations of [^{13}C] abundance in the control and study stool collections established whether unabsorbed tracer were present and whether the [^{13}C] were present in a macromolecular form (presumably incorporated into bacteria, non-dialyzable fraction) or in a small molecular form (presumably glucose or volatile fatty acids, in the dialyzable fraction, calculated by difference). The limit of detection at the dose of [^{13}C] used was 1.6% of the dose.

Calculations. Breath [^{13}C] recovered was expressed as a % of the administered dose of [^{13}C], calculated from the increase in [$^{13}CO_2$] abundance. Because CO_2 production rates were not directly measured, a CO_2 production rate of 300 mM/m^2/h was assumed. This resulted in a limit of detection of 1.8% of the administered dose (19). Body surface area was estimated by the method of Haycock *et al.* (12). [^{13}C] recovered in stool was expressed as a % of administered dose.

Infants were divided into two groups on the basis of peak H_2 production (≤20 ppm and >20 ppm) and % [^{13}C] recovered in breath and in stool after [^{13}C]-1-L were compared by *t* tests (20). Paired *t* tests were used to compare values for % dose recovered at various time points and for the 8-h area under the curve after [^{13}C]-1-G and [^{13}C]-1-L. Linear regression analysis was also used to test the relationship between H_2 excretion and % [$^{13}CO_2$] recovered and between these two variables and parameters such as lactose intake, body weight, and gestational age.

RESULTS

Validation studies. Table 1 shows the individual coefficients of correlation of the regression of [^{13}C] on [^{14}C] excretion at each time point for the seven adult subjects. Individual values for *r* varied from 0.950–0.997. The ratio of the 5-h areas under the curve of [^{13}C] to [^{14}C] ranged from 0.89–1.15, the mean (±S.D.) being 1.03 ± 0.11. These results documented the validity of using [^{13}C]-1-L for breath tests in further studies.

Table 1. *Results of validation studies of [^{13}C]-1-lactose against [^{14}C]-1-lactose in adults*

Subject	% Dose/h [^{13}C] *vs* [^{14}C] *r*	5-h area under curve [^{13}C]/[^{14}C]
1	0.983	1.08
2	0.991	1.15
3	0.997	1.13
4	0.950	1.12
5	0.997	0.91
6	0.996	0.89
7	0.996	0.96
$\bar{X}$ ± S.D.		1.03 ± 0.11

Table 2. *Percent dose recovered and cumulative % dose recovered in breath in full-term infants after [^{13}C]-1-lactose ingestion*

Time (h)	n[1]	Full-term infants: % dose/h recovered	Full-term infants: cumulative % dose recovered	Adults[2]: % dose/h recovered	Adults[2]: cumulative % dose recovered
0.5	19	0.8 ± 0.6[3]	0.2 ± 0.2		
1	19	2.2 ± 1.2	0.9 ± 0.6	1.4 ± 0.6	
1.5	9	3.8 ± 1.2	2.5 ± 1.1		
2	18	4.2 ± 1.4	4.2 ± 1.8	4.0 ± 0.9	
3	19	5.8 ± 1.3	9.2 ± 2.9	6.0 ± 0.9	
4	19	6.0 ± 1.1	14.8 ± 3.7	6.3 ± 0.9	
5	19	5.2 ± 1.0	20.7 ± 4.0	5.5 ± 0.9	
6	16	4.4 ± 1.0	26.0 ± 3.8	4.2 ± 0.9	
7	16	3.6 ± 1.0	29.9 ± 3.9	2.8 ± 0.9	30.1 ± 4.2
8	16	2.6 ± 0.8	33.0 ± 4.1		

[1] n varies due to shorter studies (5 h) in first three infants, addition of 1.5 h sample after first 10 infants had been studied, and sample tube broken in shipment.

[2] Data recalculated from Mosora *et al.* (16).

[3] Mean ± standard deviation.

Breath hydrogen. All infants had hydrogen detectable in their breath on the days of study. The peak H_2 excretion was <20 ppm in 11 infants; this was considered biologically insignificant. Eight infants were considered hydrogen excretors. Peak breath H_2 ranged from 25–158 ppm in these infants with a mean value of 76 ppm. Five of the eight hydrogen excretors had 5-h mean H_2 values greater than 20 ppm. There was no relationship of H_2 excretion to gestational age, birth weight, postnatal age or to lactose intake on the day of study.

Breath [$^{13}CO_2$] after [^{13}C]-1-L and [^{13}C]-1-G. [$^{13}CO_2$] excretion above baseline was detected in breath as early as one-half hour postprandially in 17 of the 19 infants studied and by 1 h postprandially in the remaining two. Peak [$^{13}CO_2$] excretion occurred in one infant at 2 h, in six infants at 3 h, and in nine infants at 4 h. Three infants did not reach peak excretion until 5 or 6 h postprandially. The % dose recovered per hour at various times and the cum % dose recovered (area under the curve) for all infants studied with [^{13}C]-1-L are shown in Table 2. The data are remarkably similar to those previously reported by Mosora *et al.* (16) in adults studied after a load of 95 g of maize glucose, whose natural abundance of [^{13}C] is enriched by approximately 1%, thus allowing its use as a natural label (19). The % dose per hour and the cum % dose recovered did not differ between the eight infants excreting significant amounts of hydrogen and those who were not hydrogen excretors.

Data for % dose [^{13}C] recovered per hour and cum % [^{13}C] dose recovered for the nine infants studied with both [^{13}C]-1-L and [^{13}C]-1-G are shown in Figure 1 and Figure 2. The % dose [^{13}C] recovered at each time point during the first 6 h appeared greater after [^{13}C]-G than after [^{13}C]-L, but none of the differences was significant. The cum % dose recovered from [^{13}C]-G became progressively greater than that from [^{13}C]-L at each point in time, significantly so at 6, 7, and 8 h postprandially (8 h % dose recovered: lactose, 32.6 ± 3.5% and glucose, 35.5 ± 3.1%, paired $t = 2.528$, $P < 0.05$).

Fecal excretion of [^{13}C] dose. Previous studies demonstrated that the minimum detection limit of [^{13}C] in stool was 1.6% of the dose used in these studies (18). All infants were passing stools regularly during the days of collection. Excess [^{13}C] was detected in the stool of only one infant during the 24 h after labeled glucose ingestion. The excretion was 1.9% of the dose. This infant also malabsorbed lactose.

Seventeen infants had complete reliable stool collections during the 24 h after labeled lactose ingestion. Fecal [^{13}C] excretion was >1.6% of the dose (range, 1.6–6.8%) in nine infants. Of these, eight had fecal [^{13}C] excretion >2% of the dose. There was no fecal [^{13}C] excretion above baseline during the second 24-h period after labeled lactose ingestion in the 12 infants for whom complete collections were available; this group included eight infants who had had detectable [^{13}C] on the previous day.

The mean % dose recovered in the stools of the nine infants with significant [^{13}C] excretion was 3.3%. Infants with >1.6% of the dose in their stools did not differ from infants with fecal [^{13}C] below the limits of detection with regard to body weight, lactose intake, breath hydrogen excretion, [^{13}C] recovered in breath, or stool weight.

In eight of the nine infants in whom excess fecal [^{13}C] was detected, all of it was in a dialyzable form, suggesting that it was present as a low molecular weight compound, such as lactose, glucose, or volatile fatty acids. In one of the nine infants significant

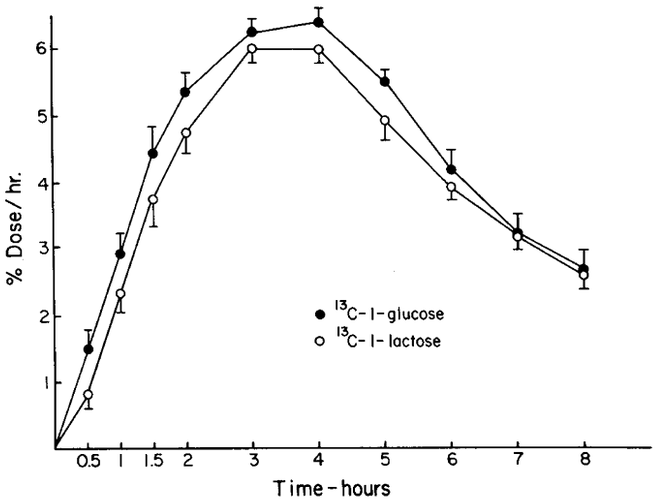

Fig. 1. Percent dose [^{13}C] recovered at various time points after ingestion of either 475 mg/m^2 of [^{13}C]-1-lactose (43 APE) or 120 mg/m^2 [^{13}C]-L-glucose (90 APE) as part of the 7 and 8 a.m. lactose-containing formula feeding (n = 9). None of the differences between [^{13}C]lactose and [^{13}C] glucose was statistically significant.

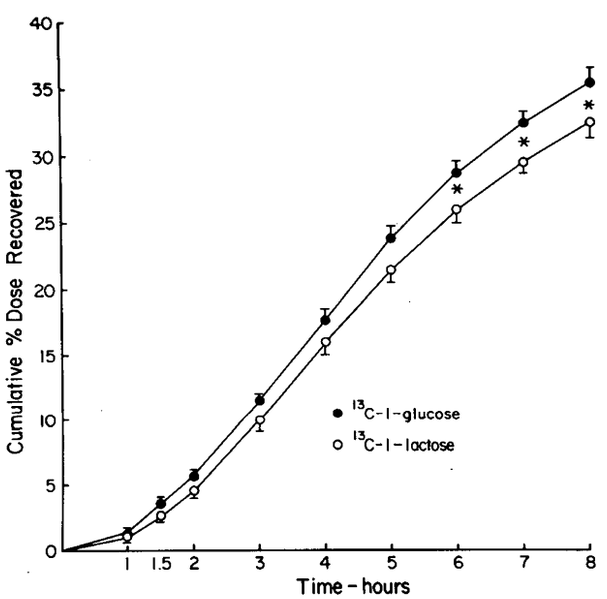

Fig. 2. Cumulative % dose [^{13}C] recovered at various time points after ingestion of either 475 mg/m^2 of [^{13}C]L-lactose (43 APE) of 120 mg/m^2 [^{13}C]L-glucose (90 APE) as part of the 7 and 8 a.m. lactose-containing formula feeding (n = 9). The values at 6, 7, and 8 h, marked with an *, were significantly different.

amounts of excess [^{13}C] (81% of that detected in stool) remained after dialysis. This finding may be interpreted to mean that the [^{13}C] had been incorporated into bacteria or some other macromolecular form, as has been suggested in studies in carbohydrate-malabsorbing adults (4). Incomplete dialysis of lower molecular weight compounds is also possible but seems less likely.

DISCUSSION

The breath and stool data from these studies imply that lactose absorption by the formula-fed full-term infant is nearly complete, even in the first week of life, and that the majority of this absorption takes place in the small intestine. Colonic salvage of carbohydrate occurs but is variable at the ages studied and appears to be quantitatively less important than is suspected in premature infants (14).

The conclusions depend on the validity of using H_2 and [$^{13}CO_2$] excretion in breath and [^{13}C] in stool as indicators of lactose absorption. Breath tests with [^{14}C]-L have been shown to differentiate between adults with high and low jejunal lactase activities documented by biopsy. The mean 4-h integrated area under the curve of [$^{14}CO_2$] excretion for adults with high lactase activity was 22.8×10^{-3}% dose/h/mM CO_2, compared to 9.9×10^{-3}% dose/h/mM CO_2 for individuals with low lactase activity (17).

Breath tests with [^{13}C]-lactose differ from H_2 breath tests in two important ways. The H_2 breath test reflects only carbohydrate that is *not* absorbed in the small intestine and that *is* fermented. The use of [^{13}C]-compounds as tracers allows measurement of what is absorbed as well as what is excreted in stool. Because only the glucose of the lactose molecule used in our studies was labeled, any interpretation of the data assumes that galactose and glucose will be absorbed at the same rate after hydrolysis. Absorption of galactose in the small intestine has actually been shown to be slightly more rapid than that of glucose (7). Absorption of [^{13}C] could occur not only in the small intestine by active transport into the enterocyte but also in the colon after fermentation, but the time course of the appearance of [$^{13}CO_2$] in breath would be expected to be different, as in suggested by the studies with [^{14}C]-L cited above (17).

A second major difference between H_2 and [$^{13}CO_2$] breath tests of importance to these studies is that each feeding of lactose gives new substrate for fermentation, making H_2 peaks somewhat difficult to interpret relative to any single feeding unless fasting thereafter is prolonged [the integrated mean of 5-h breath H_2 values was found in one study to be independent of the frequency of feeding (14)]. The test dose of [^{13}C]-L or [^{13}C]-G changes the [^{13}C]/[^{12}C] ratio in only a single feeding and the changes after ingestion can be followed for 8 h without interference from subsequent meals. The fact that the change of the *ratio* of [$^{13}CO_2$] /[$^{12}CO_2$] is measured makes the test less subject to the effects of hypoventilation or of dilution of the breath sample by room air during collection.

The time course of [^{13}C] recovery (% dose/h) and the cum % dose [^{13}C] recovered in the 19 infants studied with [^{13}C]-1-L were virtually identical to data reported in adults after a glucose load (Table 2) (16). Slight differences were noted between glucose and lactose tolerance in the subset of nine infants studied with both carbohydrates. Because the [^{13}C] label was at the C-1 position in both cases these differences most likely reflect differential rates or efficiencies of absorption rather than the rates of metabolism after absorption. In either case the differences were slight.

Analysis of the data midway through the studies had suggested that the % dose [^{13}C] recovered in breath in the first 4 h was significantly greater in infants who were not hydrogen excretors than in those excreting >20 ppm, although the 8-h recovery did not differ between the two groups. This suggested that an influx of [^{13}C] from the colon was taking place in the last 4 h of the study in hydrogen excretors. This finding did not hold up when all 19 infants were analyzed. There were no qualitative or quantitative differences in breath [^{13}C] recovery that could be related to H_2 production. This might mean that (1) only small amounts of carbohydrate reached the colon, even in H_2 excretors or (2) larger amounts of carbohydrate reached the colon in both H_2 excretors and non-excretors but that the fecal flora was incapable of fermentation in the latter group. If the second explanation were true, there should have been greater [^{13}C] excretion in the stools of infants with low breath hydrogen than in those excreting significant amounts of hydrogen. This was not the case within the limits of detection. Accordingly, we favor the first possibility.

Any conclusion must be tempered by the recognition that qualitative and quantitative differences in colonic bacteria among infants could alter markedly the relative amounts of volatile fatty acids, CO_2, and H_2 produced by fermentation. For example, the predominant pathways of fermentation by *Lactobacilli, Bifidobacterium* and *Streptococcus fecalis* produce lactate, acetate, ethanol and only limited amounts of CO_2. There is no H_2 production. *E. coli* and *Enterobacter* and *Clostridial* species, in contrast, may produce acetylphophate, butyrate, acetate, and butanol, with substantial amounts of CO_2 and H_2 being released. Nearly all *Enterobacter* have the capacity to consume H_2. Methanogenic bacteria consume both CO_2 and H_2 to produce methane and water (9). The complexities of anaerobic fermentation are beyond the scope of this discussion but the above examples demonstrate how differences in the predominant bacterial species in the colon could alter substantially the amount of H_2 produced relative to volatile fatty acids and CO_2. Furthermore, the colonization of the colon of infants delivered by Caesarian section may proceed more slowly and differ qualitatively from that seen in the infant delivered vaginally. Some discrepancy among the various parameters used to study carbohydrate absorption seems inevitable. This may also explain why reducing substances (incompletely fermented carbohydrate) are found in the stools of some infants.

Eight of 17 infants (41%) had complete absorption of lactose, *i.e.*, their fecal loss was below 1.6% of intake, the lower limit of detection. The other nine infants (59%) lost variable amounts of [^{13}C] from lactose in the stool. The average loss for all infants was 1.8% of intake. In quantitative terms this would amount to a loss of about 0.75 Kcal/kg body weight/day by an infant consuming 100 $Kcal \cdot kg^{-1} \cdot day^{-1}$ of a standard lactose-containing formula. One infant excreted 6.8% of intake, equivalent to 2.8 $Kcal \cdot kg^{-1} \cdot day^{-1}$ at 100 $Kcal \cdot kg^{-1} \cdot day^{-1}$. Neither loss would be of major nutritional significance.

Bond and Levitt (5) have studied the efficiency of colonic metabolism of carbohydrate in adult volunteers in whom [^{14}C]-glucose was instilled into the colon. A mean of 14% of a 12.5 g dose was subsequently excreted in the stools. Of this an average of 17% was dialyzable, the other 83% having been converted into a non-dialyzable form. In a subsequent study of four patients with jejunoileal bypass fed [^{14}C]-sucrose, 42% of the label not absorbed in the small bowel was subsequently excreted in the stool, of which 33% of it was in a dialyzable form (4). The stools of only one of the nine infants who excreted detectable amounts of label in the stool in our study contained [^{13}C] in a non-dialyzable form. At this age most of the labeled carbohydrate lost was in a dialyzable and osmotically active form.

These studies were limited to the first 10 days of life and provide no information on the changes in lactose digestion that may take place in the first 3–4 months of life. Rapid growth of the intestine during the first 48 h of life has been demonstrated in lower animals fed colostrum and their mother's milk (13, 22). The same may occur in the human infant. During the early months of life there is rapid weight gain and linear growth. The absolute intake of lactose increases substantially in the first 3–4 months of life. Preliminary data have suggested that maximum H_2 excretion occurs at about 8 wk of age (3). Whether this is a consequence of changes in dietary intake, in lactase levels, or in fecal flora has not been determined.

Finally, it is clear from these studies, as it was from studies of premature infants (14), that elevated breath H_2 measurements cannot be equated with lactose intolerance in any symptomatic sense. The application of the breath H_2 test to older children and adults is appropriate if the question to be answered is whether

there is some degree of small intestinal carbohydrate malabsorption present. An abnormal test does not imply the necessity of removing the carbohydrate in question from the diet, a logic that would require removal of milk from the diet of nearly all infants. Decisions on dietary management are still best made on clinical grounds.

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29. Enfamil (Mead Johnson). Lactose content 7% W/Vol. This formula was used because it produced little change of the baseline ratio $^{13}CO_2/^{12}CO_2$ in breath after feeding (17).

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