I-1369

Original Research Communications—general

# Dietary manipulation of postprandial colonic lactose fermentation: I. Effect of solid foods in a meal[1-3]

Noel W Solomons, MD, Aura-Marina Guerrero, and Benjamin Torun, MD, PhD

ABSTRACT The effect of adding solid foods—cornflakes, banana and hard-boiled egg—to a meal with 360 ml of intact milk containing 18 g of lactose was investigated in 13 lactose-malabsorbers and 10-lactose-absorbers chosen from 36 Guatemalan adults screened for their capacity to digest and absorb completely the lactose in this volume of milk. A six-hour hydrogen breath test was used as the index of carbohydrate absorption. Minimal breath $H_2$ was excreted by lactose-absorbers with either the intact milk alone, the intact milk with solid foods, or lactose-prehydrolyzed milk with solids. In lactose-malabsorbers, however, the 6-h excretion of $H_2$ with intact milk plus solid food was intermediary between milk alone and prehydrolyzed milk with solids. A relative net reduction of 47% in lactose malabsorption was produced by adding food, and the peak-rise in breath $H_2$ was delayed by 2 hours. A physiological consequence of taking solid foods along with milk is a slower rate of colonic fermentation, and this may be the basis for reducing gastro-intestinal symptoms in lactose-intolerant malabsorbers. *Am J Clin Nutr* 1985; 41:0000–0000.

KEY WORDS lactose, hydrogen breath test, intestinal absorption, intestinal transit time, dietary fiber, lactase deficiency

## Introduction

A large portion of the world's population has genetically-determined lactase deficiency (1). Thus, with advancing age, the mucosal content of lactase is progressively reduced such that lactase levels are generally below 3 IU/g wet weight by late childhood and thereafter (2). Diminished enzyme levels result in less efficient hydrolysis of the milk sugar, lactose. The conventional diagnostic procedure—the lactose tolerance test—involves the administration of a concentrated solution containing 50 g of lactose, equivalent to the sugar content of a full liter of cow's milk. Such a procedure stresses the limits of the digestive capacity of lactase-deficient individuals, and usually over 70% will experience gastrointestinal symptoms including abdominal distension, cramps, eructations, flatulence, and/or watery stools, symptoms that result from the bacterial fermentation of carbohydrates with the evolution of gases ($CO_2$, $CH_4$, $H_2$) and osmotically-active organic acids (3). By contrast, *dietary* amounts of lactose, ie. the quantity in a glass of milk, that is 12 g, usually are well-tolerated by most lactase-deficient individuals (4–9), but severe gastrointestinal symptoms are attendant to the malabsorption of even small amounts of lactose by some individuals (10, 11).

Milk represents a rich source of several nutrients including calcium and riboflavin. It is also an indispensible component of meals containing puddings, custard, ice

[1] From the Institute of Nutrition of Central America and Panama, Guatemala City, Guatemala, and the Department of Nutrition and Food Science, Massachusetts Insutute of Technology, Cambridge, MA, 02139.

[2] INCAP Publication: I-1369.

[3] Address reprint requests to: Noel W Solomons, MD Division of Nutrition and Health INCAP Carretera Roosevelt, Zona 11 Guatemala, Central America, AP 11-88.

Received April 12, 1984.

Accepted for publication September 12, 1984.

cream, and ready-to-eat breakfast cereals. Enabling milk-intolerant lactose-malabsorbers to use appreciable amounts of milk and dairy products in their diets would provide nutritional benefits and greater diversity in food selection. Several strategies to overcome lactose intolerance and milk rejection have been conceived. Most are based on the reduction of the lactose content of milk through enzymatic hydrolysis of the lactose (12, 13) or ultrafiltration (14). Simpler, more direct, approaches to the intolerance to usual dietary levels of lactose, however, would be useful additions to the overall effort to reduce milk avoidance. The adding of fiber components to milk is one of the more imaginative recent contributions in this direction (15).

It has been anecdotally reported that combining milk into a meal with solid foods reduces or eliminates symptoms that would otherwise be experienced if a given individual consumed the same volume of milk alone as a beverage. The physiological bases for this claim, however, have not been firmly established. We have speculated that the rate of transit of lactose through the stomach and small intestine could be a major determinant of the subjective symptoms that attend milk ingestion by an intolerant malabsorber (16). In the present study, we have used the hydrogen ($H_2$) breath-analysis test as an index of incomplete carbohydrate absorption to evaluate the physiological consequences of combining milk with solid food elements in adult lactose malabsorbers.

## Subjects and Methods

### *Subjects*

Thirty-six individuals, ranging in age from 19 to 50 yr, 6 males and 30 females participated in the screening phase of the study. The purpose of the screening was to identify an available pool of volunteers characterized in terms of their capacity to digest lactose for derivative experiments with various intervention procedures. All were healthy, without history or symptoms of chronic gastrointestinal illness and not receiving oral antibiotics. Individuals who both affirmed and denied previous milk intolerance were enrolled into the study. All subjects agreed to participate in the study after the risks and benefits had been fully explained, and informed consent had been obtained. The protocol had been approved by the Committee on the Use of Humans as Experimental Subjects of MIT and the Human Rights Committee of INCAP.

### *Collection of Expired Air and Analysis of Hydrogen*

The breath collection technique was a modification of our procedure previously described for children (17, 18). Samples of mixed pulmonary gas were obtained by having the subjects breathe normally through a one-way Hans Rudolph valve (Warren Collins, Braintree, MA) into a 5-L rubber anesthesia bag with nipple (Warren Collins) until over 3 L of air had been collected. After flushing the dead-space in the nipple and connector, 30 to 60 cc of air from the bag were transferred into a plastic syringe fitted with a three-way stopcock. Samples stored in this manner lose 5% of their $H_2$ concentration per 24 h (19). All samples were measured within 8 h of collection.

Samples were analyzed for $H_2$ concentration on a compact, thermal conductivity detection gas-solid chromatographic apparatus (MicroLyzer Model-12, Quintron Instruments Co, Milwaukee, WI) with a digital display meter and using room-air compressed by an internal pump as the carrier gas (20, 21). The machine was calibrated using one or another of two standard reference gases of known $H_2$ concentration (Scotty Gas II, Supelco, Bellefonte, PA; Linde Gas, Linde Division of Union Carbide, N Chicago, IL); the two gas mixtures were internally standardized. Once calibrated, the MicroLyzer registers the concentration of a sample of gas—reference standard or unknown—on a digital display panel in parts per million (ppm).

### *Absorption Breath Tests*

All 36 subjects were initially screened for their lactose absorption capacity using an ordal dose of 360 ml of intact, whole cow's milk (IM) (La Pradera, Guatemala City, Guatemala). Herein, bovine milk has been assumed to contain 5% lactose (w/v); thus, the volume of milk of our test dose provided 18 g of carbohydrate in the form of lactose. Breath samples in the screening test were taken at 30-min intervals over a 6-h period. For uniformity and consistency with the subsequent studies, only data at 60-min intervals have been computed in the present study.

A rise in breath $H_2$ concentration of $\geq$25 ppm above th fasting level at any hourly breath-collection interval following the milk dose was the criterion for classification as a lactose-malabsorber. Individuals with increments below this criterion were classified as lactose-absorbers. The conventional cut-off criterion that signifies biologically-significant incomplete absorption of oral carbohydrate is an increment in breath $H_2$ of $\geq$20 ppm (22), but here we sought to enroll a population of malabsorbers with greater excess $H_2$ excretion for inclusion in the derivative protocol studies in this paper, and in the companion article (23), involving potentially beneficial interventions.

Ten subjects classified as lactose-absorbers agreed to participate, and from our pool of lactose-absorbers we chose 13 willing volunteers to enroll roughly equivalent numbers of individuals in the comparative studies with a standard breakfast meal. The meal consisted of 40 g of cornflakes (Kellogg Co, Battle Creek, MI), a hard-boiled egg, and a medium banana. Subjects were studied on two occasions in a randomized order, separated by at least 48 h to avoid the effects of residual colonic

acidification (24). On one occasion, the meal was accompanied by 360 ml of lactose-prehydrolyzed milk (HM), preincubated for 24 h with 0.25 g of LactAid (LactAid Co, Pleasantville, NJ), a commercial, food-grade beta-galactosidase enzyme preparation derived from *Kluyveromyces lactis*. This treatment has been reported to produce >90% hydrolysis of lactose to glucose and galactose (13), and in our laboratory, incubation of milk formula with the appropriate dosage consistently produced net hydrolysis of >99% (25).

*Data analysis*

Descriptive statistics were calculated based on the change in breath $H_2$ concentration and on the area under the discontinuous curve of breath $H_2$ concentration expressed in ppm · hr (26), an expression similar to that used by others (27, 28). Differences between treatments were compared using the Student *t* test with a probability of $p < 0.05$ considered to be significant.

## Results

### *Postmilk hydrogen excretion by lactose-absorbers and lactose-malabsorbers*

Of the total of 36 screening tests performed for this study and a subsequent investigation (23), 12 individuals had maximum increments in breath $H_2$ concentration above baseline of <25 ppm after consuming 360 ml of IM, and were classified as lactose-absorbers. The remaining 24 subjects manifested a rise in $H_2$ of ⩾25 ppm, and were classified as lactose-malabsorbers. The mean peak-rise after intact milk in the lactose-absorbers was 7.1 ± 2.0 ppm (mean ± SEM), whereas that for the lactose-malabsorbers was 35.2 ± 2.7 ppm. Composite curves of the mean hourly changes in breath $H_2$ concentration attendant to the IM screening test for the whole group are shown in **Figure 1.** It would be expected that any intervention favorable to the reduction in the rate of delivery or the total delivery of unabsorbed carbohydrate to the colon in lactose-malabsorbers would be characterized by a change in the composite breath $H_2$ curve for that group from that shown (upper curve, Fig 1) *toward* the one generated by the lactose-absorbers (lower curve, Fig 1).

### *Effect of solid food on hydrogen production from intact and lactose-hydrolyzed milk*

Twenty-three individuals—10 lactose-absorbers and 13 lactose-malabsorbers—participated in the protocol that involved the standard test-meal along with 360 ml of either IM or HM as the beverage. The mean interval breath $H_2$ concentrations for the two groups over the 6 h following the standard meal with both beverages are shown in **Figure 2.** It can be appreciated that the consumption of the meal with IM by the lactose-malabsorbers led to the excretion of substantially more pulmonary $H_2$ than with the other forms of milk. The $H_2$ excretion-volume after the meal plus HM in the malabsorbers and after the meal plus either beverage in the absorbers are not significantly different.

### *Comparison of colonic carbohydrate fermentation with fluid milk alone, or milk plus solid foods*

In **Figure 3,** the magnitude and time-course of the breath $H_2$ responses for intact milk taken alone or taken along with solid foods is shown for the 13 lactose-*malabsorbers*. As shown in the upper graph of Figure 3, the total area under the discontinuous curve of breath $H_2$ concentration was greater with milk alone over the 6-h interval. However, as some of the $H_2$ in the test with the milk plus solid food could have come from colonic fermentation of the non-absorbable carbohydrate (dietary fiber) in the cereal or fruit, we corrected the data for the standard meal studies by subtracting the $H_2$ curve produced with the meal plus HM for each individual. Thus, in the lower graph of Figure 3, the *change* in breath $H_2$ concentration (using the baseline, fasting sample as reference) is displayed, and the excess $H_2$ excretion plotted, corrected for the contribution from cereal and fruit in the meal-derived curve. Consuming 360 ml of IM with a meal reduced the amount of lactose reaching the colon during the 6-h postprandial period by 47%. Moreover, the average peak-rise in breath $H_2$ was displaced from the third post-prandial hour with liquid IM alone to the fifth post-prandial hour with IM plus solid food.

## Discussion

It has been a frequent contention that milk is better tolerated by lactase-deficient individ-

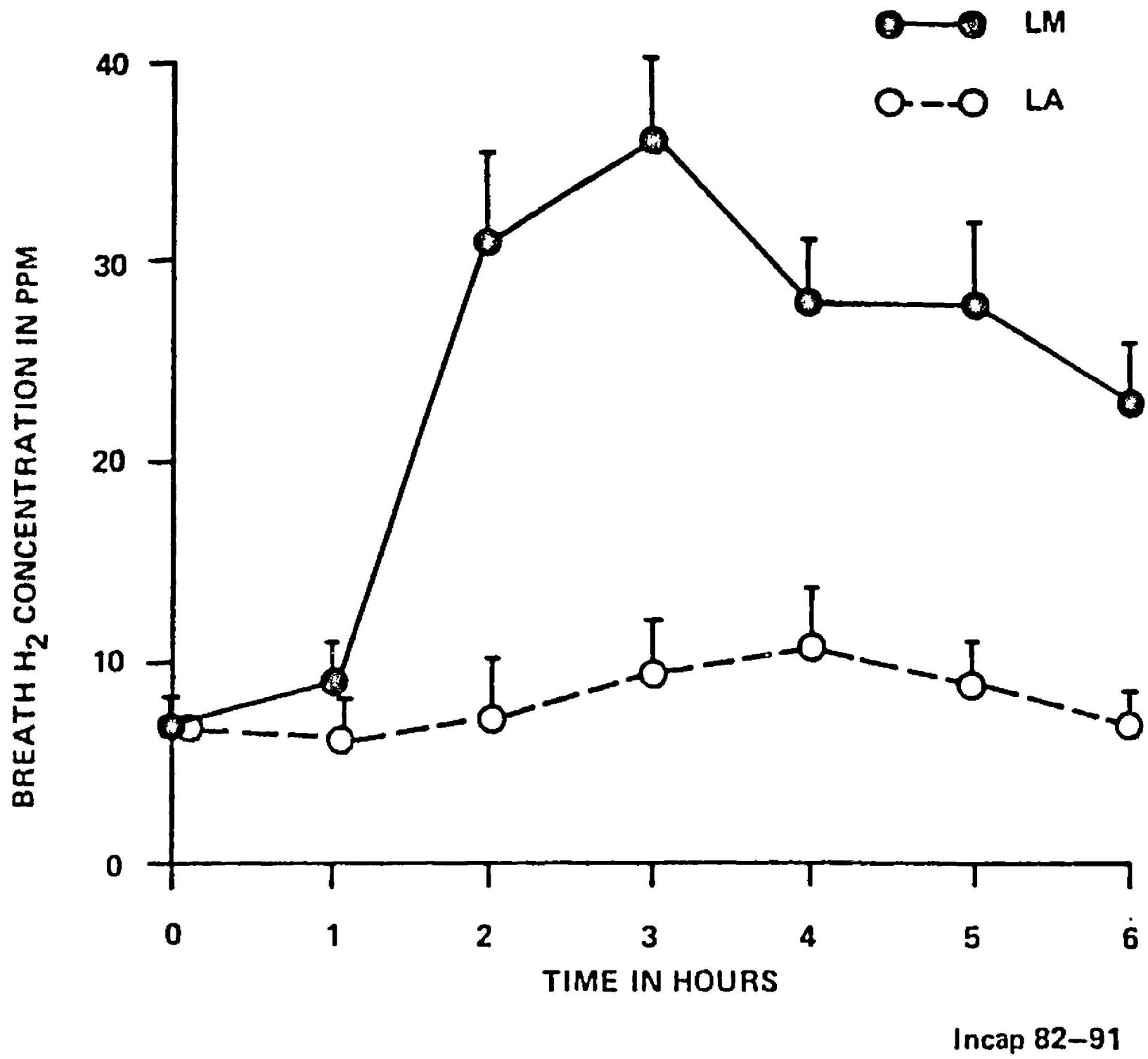



FIG 1. Mean breath $H_2$ concentration (±SEM) in ppm at 60-min intervals over 6 h in 24 lactose-malabsorbers and 12 lactose-absorbers after the ingestion of 360 ml of intact milk.

uals when combined with food than when drunk alone. In an extreme demonstration, Garza and Scrimshaw (5) observed almost no symptoms when lactose-malabsorbing children were fed 12 g of lactose mixed into a sandwich. Since the symptoms of lactose intolerance derive from the arrival of lactose in the colon, carrying water from the small intestine and provoking fermentation by the colonic flora and the evolution of gases and osmotically-active cleavage products (3), we felt that monitoring the rate and extent of *in vivo* colonic fermentation after consuming lactose would provide a physiological correlate of the passage of unabsorbed carbohydrate into the colon. Whether $H_2$ evolution per se is a major contributor to the syndrome of carbohydrate intolerance is controversial (29), but the pulmonary excretion of $H_2$ suggests itself as a useful marker of colonic fermentation of unabsorbed substrate. It has proven useful in differentiating the effects of various manipulations of milk and lactose digestion and absorption (30). The $H_2$ breath test is non-invasive, ideal for use in healthy volunteers. It has a high sensitivity and specificity for diagnosing lactase deficiency (31), assuring that our classification of our 36 initial subjects into the respective categories of lactose-malabsorber and lactose-absorber is highly reliable. It is sensitive enough to detect the incomplete absorption of only

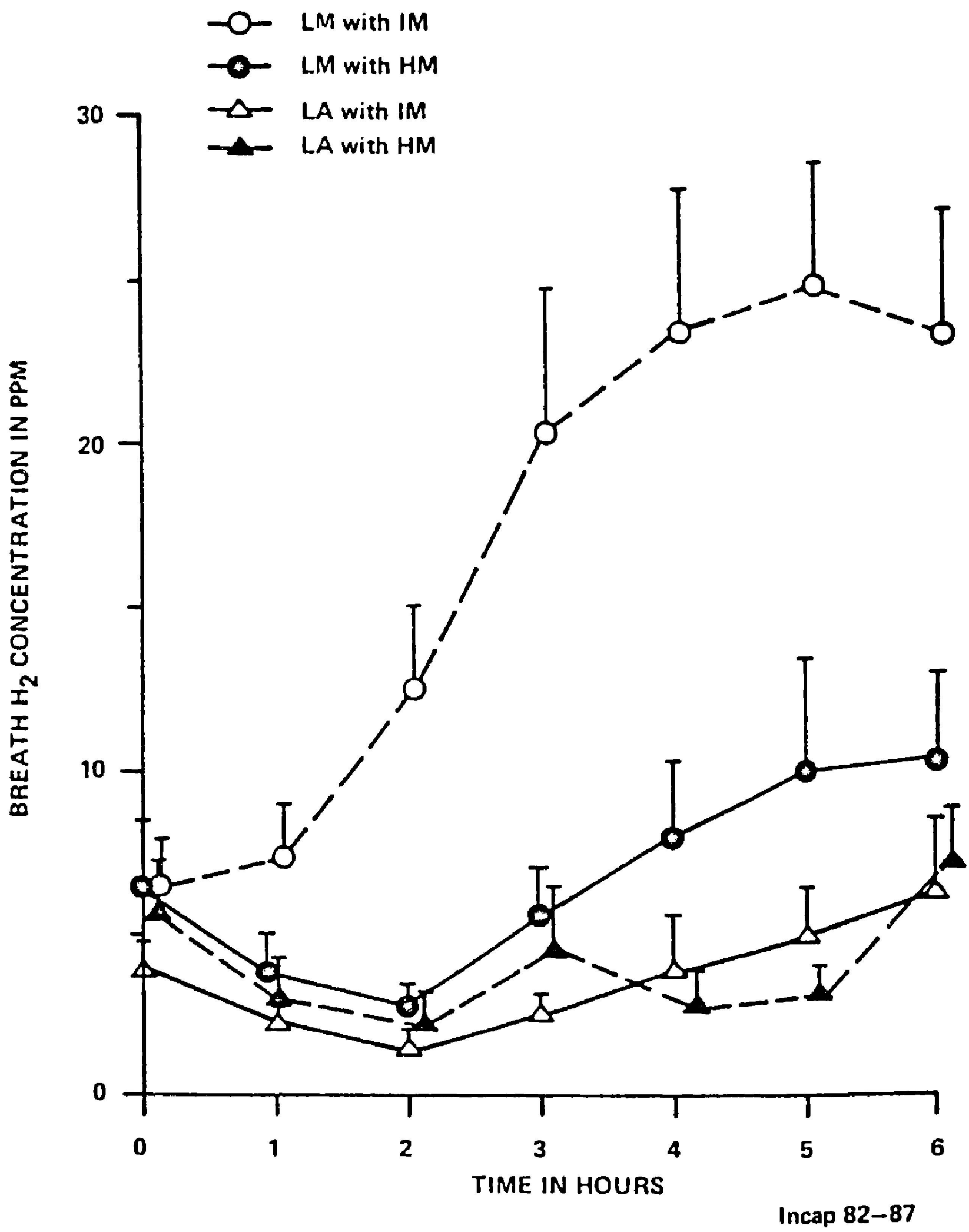
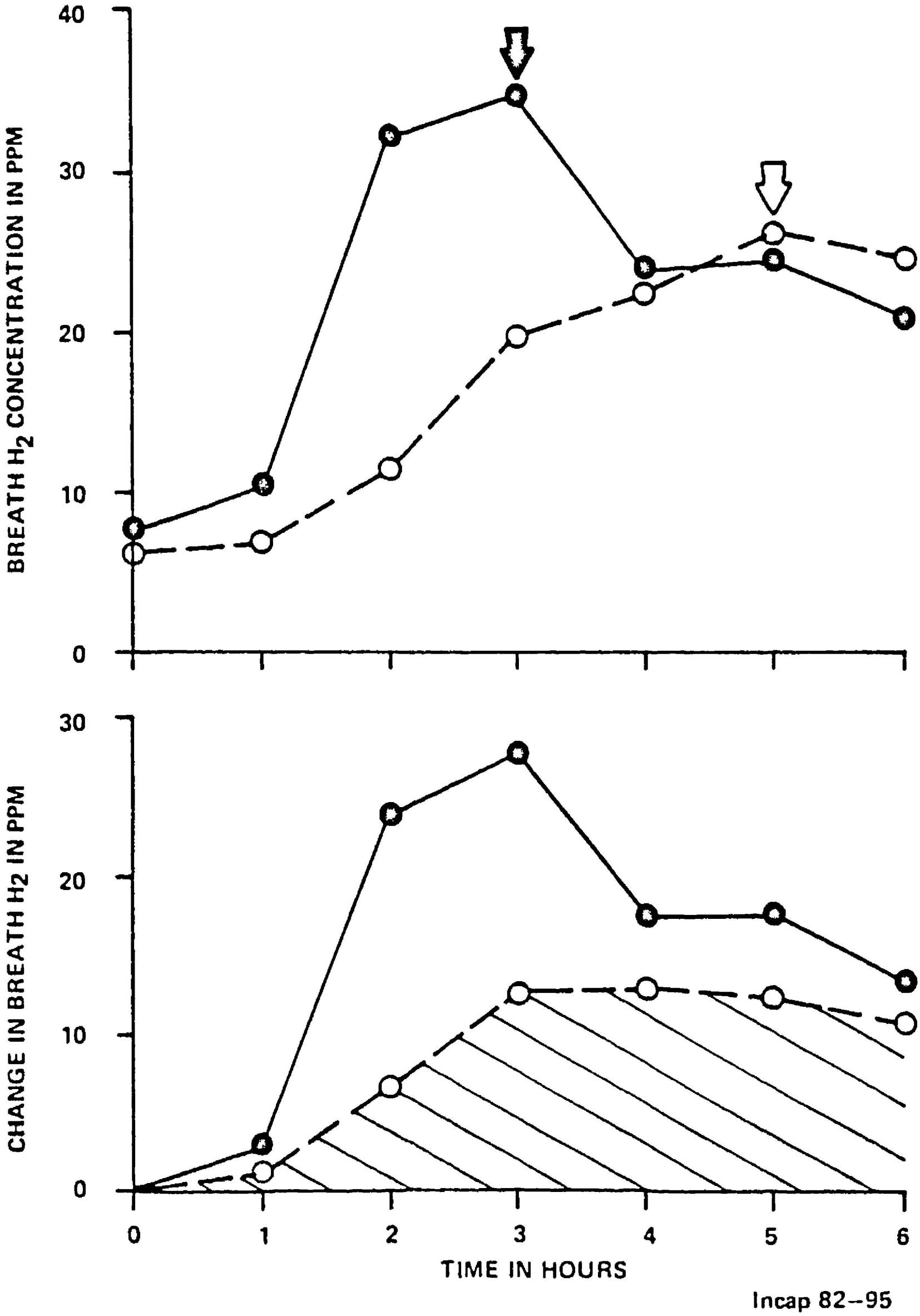



FIG 2. Mean breath $H_2$ concentration (±SEM) in ppm at 60-min intervals over 6 h after ingestion of a standard meal with intact milk or hydrolyzed milk by 13 lactose-malabsorbers and 10 lactose-absorbers.

small amounts of substrate from physiological doses of lactose (32, 33). Although usually applied in a clinical context (22), a number of investigators have used the $H_2$ breath test to study the efficiency of carbohydrate absorption from various foodstuffs including:


BREATH $H_2$ CONCENTRATION IN PPM
40
30
20
10
0
CHANGE IN BREATH $H_2$ IN PPM
30
20
10
0
0
1
2
3
4
5
6
TIME IN HOURS

Incap 82--95

milk and dairy products (7, 8, 15, 16, 23, 27, 29, 33–45); beans (46–48); vegetables and fruits (49, 50) and cereal grains and starches (7, 8, 51–56). We thus felt that this approach was most suitable for the selection of a subsample of lactose-malabsorbers, as well as for determination of the physiological concomitants of consumption of a dietary amount of milk, with and without solid foods. Our dosage of lactose—18 g—is larger than that in the 8 oz glass of milk (12 g) often used as the standard of typical consumption (9), but it closely approximates usual *meal* situations in which a glass of milk might accompany a serving of cottage cheese, creamed soup, cream sauce, ice cream, or, as in our study, a bowl of ready-to-eat cereal and milk.

That the $H_2$ response in lactose-malabsorbers following the consumption of meal of 360 ml of intact milk plus a refined ready-to-eat breakfast cereal, banana and egg is largely due to the incomplete absorption of the carbohydrate in milk, lactose, was demonstrated conclusively by the major reduction in excess pulmonary excretion of $H_2$ when a lactose-prehydrolyzed milk was substituted for intact milk. As expected, efficient lactose-absorbers handled the lactose-containing and low-lactose meals in an identical fashion with no pronounced $H_2$ response following either offering. Although the mean concentration of breath $H_2$ was never significantly higher than fasting with HM plus the meal when fed to lactose-malabsorbers, or with either form of milk plus the meal in the absorbers, a clear upward drift in breath $H_2$ concentration from the postprandial nadir at 2 h to the latter hours of the test can be appreciated (Fig 2). We attribute this $H_2$ to the colonic fermentation of small amounts of the other carbohydrates in the solid elements of the meal. Dietary fiber, as contained in the bananas, can produce an $H_2$ response (51, 52), and even refined flour can contribute to colonic fermentation (8, 53). In some individual subjects, in fact, this contribution of non-absorbed, non-lactose carbohydrate was quite substantial. Thus, in the context of a solid meal, we felt obliged to consider the *lactose* effect as the $H_2$ produced with the meal plus IM *minus* the $H_2$ production with the meal plus HM.

When the pattern of postprandial breath $H_2$ excretion in the lactose-malabsorber group is compared for intact milk alone and the same volume of milk consumed with the standard breakfast meals, a striking difference is noted. The excretion of $H_2$ rises steadily, reaching its peak at 3 h after the meal with the milk alone. At this time-point, mean breath $H_2$ concentration is 15 ppm higher than at a comparable time after the milk plus a meal. With the solid foods, the peak of colonic fermentation occurs two hours later, at 5-h postprandial. Moreover, when the areas under the curves of the change in breath $H_2$ concentration are calculated, there is a 47% reduction in the contribution to colonic fermentation from lactose during the 6 h postprandial when the milk was taken along with solids. Since the collection period was terminated after the sixth hour in order that the subjects could eat their lunch, we cannot know whether net $H_2$ excretion from the two treatments would have further approximated one another over the course of the next 6 to 8 h, for example.

If we assume that the *rate* of colonic arrival of non-absorbed carbohydrate and the intensity of malabsorption and fermentation per unit time are differential factors in the experience of adverse gastrointestinal symptoms such as bloating and distension, cramping, and diarrhea, then the distinct kinetic patterns of lactose-related $H_2$ production would serve as a reasonable *physiological* explanation for a reduction in symptomatology when milk

FIG 3. (Upper graph) The mean breath $H_2$ concentrations at 60-min intervals over 6 h in 13 lactose-malabsorbers after ingestion 360 ml of intact milk: alone (— ● —); or with the standard meal (— O —). The arrows represent, respectively, the postprandial hour when the greatest amount of total breath $H_2$ excretion was occurring following the milk beverage alone (black arrow, 3rd hour) and the milk with the meal (white arrow, 5th hour).] (Lower graph) The mean *changes* in breath $H_2$ concentrations at the same intervals in the same individuals and experiments with the same respective symbols, but with the $H_2$ excretion following the meal corrected for the rise in $H_2$ related to the fermentation of other carbohydrates in the solid foods by subtracting the interval changes in breath $H_2$ from each individual's meal with *lactose-hydrolyzed* milk (shaded area) (see text).

was consumed with a meal. Unfortunately, although symptoms were recorded with the dose of IM alone, no comparable, systematic recording of symptoms was conducted with the meal treatment. Thus, our present experiments cannot confirm or refute an improved subjective tolerance of milk when it is consumed with solids.

The mechanisms by which solid foods reduce the arrival in the colon of nonabsorbed lactose could be multiple. A logical factor would be a slowing of the overall mouth-to-colon transit due to a reduction in the rate of gastric emptying. Indeed, we found a slower rate of $H_2$ production after a dose of lactose provided as whole milk, compared to an aqueous lactose solution, in preschool children (16). Similarly, using breath $H_2$ analysis, Ellestad-Sayed et al (41) studied the effect of meals on the evolution of gas following milk consumption in Manitoba Indian schoolchildren; the production of $H_2$ was greater after skim milk alone than after skim milk plus a sandwich, but this relationship did not hold with diluted evaporated whole milk as the test beverage. The reduced fermentation and slowed time-course of breath $H_2$ concentration rise produced in adult Guatemalan lactose-malabsorbers when the meal was taken with milk could be the simple consequence of the retarding effects on gastric emptying of the additional 5.7 g of fat and 10 g of protein in the solids (57).

In addition to delayed transit per se, the slower flow of lactose through the small bowel might allow for a greater magnitude of hydrolysis by the residual endogenous intestinal lactase in these lactase-deficient individuals. The possibility that slower transit rates actually increase *net digestion* of lactose is suggested by observations of Leichter (58). Using the change in blood glucose as the index of lactose digestion, he noted an increasing area under the glucose curve as the lactose-malabsorbing subjects progressed from aqueous lactose to skim milk to whole milk at a lactose dosage of 50 g, suggesting improved assimilation of the sugar.

The observations on fiber components from Oklahoma (15, 59) add a fresh perspective on physiological mechanisms. Nguyen et al (15) compared breath $H_2$ responses and symptoms in 6 lactose-malabsorbers who ingested 24 g of lactose in either a 480 ml aqueous solution or as 480 ml of whole milk. The effect of adding various components of dietary fiber was investigated. Psyllium, but not cellulose enriched bread nor pectin, produced a significant reduction in $H_2$ excretion and intolerance. The authors could not explain the unique effect of psyllium in terms of differential influences on gastric emptying rate or mouth-to-colon transit time. A similar influence of psyillium on $H_2$ production after glucose in gastrectomy patients has also been reported (59). A *direct* effect of the psyllium hydrophilic mucilloid on pulmonary excretion of $H_2$ cannot be excluded. Activated powdered charcoal, for instance, has been shown to attentuate the appearance of $H_2$ in expired air after a meal of beans, presumably by adsorption of the gas in the colon (48). The effect of psyllium, and perhaps part of the effect of our standard meal, could relate to adsorption or trapping in the colon of the $H_2$ produced by the fermentation of lactose.

Recent observations demonstrate that not all of the carbohydrate that escapes removal by the small intestine is lost to the economy of the organism. If osmotic forces and fluid accumulation do not overwhelm the large bowel, an efficient colonic conservation of energy is possible (60–63). The reduced rate of postprandial fermentation of lactose, when milk is consumed with a meal, may serve both to reduce the intensity of symptoms and to improve the efficiency of colonic conservation of dietary energy from nonabsorbed carbohydrate.

Milk is rich in several nutrients of importance to adult nutrition (64). The willingness to consume milk and dairy products also provides for greater diversity in dietary selection. For individuals with primary lactase deficiency, the margin between milk intolerance and rejection, and the comfortable, regular consumption of milk could be determined by the presence of a solid meal. The present study provides a physiological perspective on the anecdote that taking milk with solid foods improves tolerance in lactase-deficient persons; we have demonstrated that certain foods—breakfast cereal, egg, and banana—reduce the postprandial colonic fermentation in response to 12 oz of milk in lactose-malabsorbers by about one-half.

We acknowledge the donation of product (LactAid) from the LactAid Co, Pleasantville, NJ. The MicroLyzer Model 12 gas chromatograph was donated by the Quintron Instruments Co, Milwaukee, WI.

## References


1. Simoons FJ. Geographic pattern of primary adult lactose malabsorption: a further interpretation of evidence of the Old World. In: Paige DM, Bayless TM, eds. Lactose Digestion: Clinical and Nutritional Implications. Baltimore, The Johns Hopkins University Press, 1981:23–48.
2. Flatz G, Rotthauwe HW. The human lactase polymorphism: Physiological and genetics of lactose absorption and malabsorption. Prod Med Genet 1977;2:205–49.
3. Christopher NL, Bayless TM. Role of the small bowel and colon in lactose-induced diarrhea. Gastroenterology 1971;40:845–52.
4. Newcomer AD, McGill DB, Thomas PJ, Hofmann AF. Tolerance to lactose among lactose-deficient American Indians. Gastroenterology 1978;74:44–6.
5. Garza B, Scrimshaw NS. Relationship of lactose intolerance to milk intolerance in young children. Am J Clin Nutr 1976;29:192–6.
6. Stephenson LS, Latham MC. Lactose intolerance and milk consumption: the relation of tolerance to symptoms. Am J Clin Nutr 1974;27:296–303.
7. Brown KH, Khatun M, Parry L, et al. Nutritional consequences of low dose milk supplements consumed by lactose-malabsorbing children. Am J Clin Nutr 1980;33:1054–63.
8. Calloway DH, Chenoweth WL. Utilization of nutrients in milk- and wheat-based diets by men with adequate and reduced abilities to absorb lactose. I. Energy and nitrogen. Am J Clin Nutr 1973;26:939–51.
9. Newcomer AD. Immediate symptomatic and long-term nutritional consequence of hypolactasia. In: Paige DM, Bayless TM, eds. Lactose Digestion: Clinical and Nutritional Implications. Baltimore: The Johns Hopkins University Press, 1981:124–33.
10. Bendine MS, Bayless TM. Intolerance of small amounts of lactose by individuals with low lactase levels. Gastroenterology 1973;65:735–43.
11. Gudmand-Høyer E, Simony K. Individual sensitivity to lactose in lactose malabsorption. Am J Dig Dis 1977;22:177–81.
12. Kosikowski FV, Weirzbicki LE. Lactose hydrolysis of raw and pasteurized milk by *Sacchromyces lactis* lactase. J Dairy Sci 1972;56:156–50.
13. Rand AG Jr. Enzyme technology and the development of lactose-hydrolyzed milk. In: Paige IM, Bayless TM, eds. Lactose Digestion: Clinical and Nutritional Implications. Baltimore, The Johns Hopkins University Press, 1981:219–30.
14. Lybeck-Sorensen K, Vergara-Meersohn M, Larsen L, et al. A new low lactose skimmed milk powder. XII International Congress of Nutrition, San Diego, Abstracts. 1981:72 (abstr).
15. Nguyen KN, Welsh JD, Manion CV, Ficken VJ. Effect of fiber on breath hydrogen response and symptoms after oral lactose in lactose malabsorbers. Am J Clin Nutr 1982;35:1347–51.
16. Solomons NW, Gracía-Ibañez R, Viteri FE. Reduced rate of breath hydrogen ($H_2$) excretion with lactose tolerance tests in young children using whole milk. Am J Clin Nutr 1979;32:783–6.
17. Solomons NW, Viteri FE, Hamilton LH. Application of a simple chromatographic technique for measuring breath hydrogen. J Lab Clin Med 1977;90:856–62.
18. Solomons NW, Rosenberg IH, Viteri FE. Development of an interval sampling hydrogen ($H_2$) breath test for carbohydrate malabsorption in children: Evidence for a circadian pattern of breath $H_2$ concentration. Pediatr Res 1978;12:816–23.
19. Rosado JL, Solomons NW. Storage of hydrogen breath-test samples in plastic syringes (letter). Clin Chem 1983;29:583–4.
20. Christman NT, Hamilton LH. A new chromatographic instrument for measuring trace concentrations of breath hydrogen. J Chromatog 1982;229:259–65.
21. Solomons NW, Hamilton LH, Christman NT, Rothman D. Evaluation of a rapid breath-hydrogen analyzer for clinical studies of carbohydrate absorption. Dig Dis Sci 1983;28:397–402.
22. Solomons NW. Diagnosing and screening technique for lactose maldigestion: Advantages of the hydrogen breath test. In: Paige DM, Bayless TM. eds. Lactose Digestion: Clinical and Nutritional Implications. Baltimore: The Johns Hopkins University Press, 1981:91–109.
23. Solomons NW, Guerrero A-M, Torun B: Dietary manipulation of postprandial colonic lactose fermentation. II. Addition of exogenous, microbial beta-galactosidases at mealtime. Am J Clin Nutr 0000;00:000–000.
24. Perman JA, Modler, S, Olson AC. Role of pH in production of hydrogen from carbohydrate by colonic bacterial flora: Studies in vivo and in vitro. J Clin Invest 1981;67:643–50.
25. Solomons NW, Torun B, Caballero B, Flores-Huerta S, Orozco G. The effect of dietary lactose on the early recovery from protein-energy malnutrition. I. Clinical and anthropometric indices. Am J Clin Nutr 1984;40:000–000 (Sept 1984)
26. Solomons NW, García R, Schneider R, et al. $H_2$ breath test during diarrhea. Acta Scand Paediat 1979; 68:171–2.
27. Ravich WJ, Bayless TM, Thomas M: Fructose: Incomplete intestinal absorption in humans. Gastroenterology 1983;84:26–9.
28. Welsh JD, Payne DL, Manion C, Morrison RD. Interval sampling of breath hydrogen ($H_2$) as an index of lactose malabsorption in lactase-deficient subjects. Dig Dis Sci 1981;26:681–5.
29. Lasser RB, Bond JH, Levitt MD. The role of intestinal gas in functional abdominal pain. New Engl J Med 1975;293:524–5.
30. Payne DL, Welsh JD, Manion CV, et al. Effectiveness of milk products in dietary management of lactose malabsorption. Am J Clin Nutr 1981;34:2711–5.
31. Newcomer AD, McGill DB, Thomas PJ, Hofman AF. Prospective comparison of indirect methods for detecting lactase deficiency. New Engl J Med 1975;293:1232–5.

32. Bond JH, Levitt MD. Quantitative measurement of lactose absorption. Gastroenterology 1976;70:1058–61.
33. Solomons NW, Gracía-Ibanñex R, Viteri FE. Hydrogen breath test of lactose absorption in adults: The application of physiological doses of whole cow's milk sources. Am J Clin Nutr 1980;33:545–54.
34. Calloway DH, Murphy EL, Bauer D. Determination of lactose intolerance by breath analysis. Am J Dig Dis 1969;19:811–5.
35. Gearhart HL, Bose DP, Smith CA, et al. Determination of lactose malabsorption by breath analysis with gas chromatography. Anal Chem 1976;48: 393–8.
36. Caskey DA, Payne-Bose D, Welsh JD et al. Effects of age on lactose malabsorption in Oklahoma Native Americans as determined by breath $H_2$ analysis. Am J Dig Dis 1977;22:113–6.
37. Payne-Bose D, Welsh JD, Gearhart HL, et al. Milk and lactose hydrolyzed milk. Am J Clin Nutr 1977; 30:695–7.
38. Fernandes J, Vos CE, Douwes AC, et al. Respiratory hydrogen excretion as a parameter for lactose malabsorption in children. Am J Dis Child 1978;31:597–602.
39. Rorick MH, Scrimshaw NS. Comparative tolerance of elderly from different ethnic backgrounds to lactose-containing and lactose-free dairy drinks: a double-blind study. J Gerentol 1979; 34:191–6.
40. Solomons NW, García-Ibañez R, Aycinena P, et al. Lactose intolerance in protein-energy malnutrition: a clinical case study and family study using a hydrogen breath-analysis test for carbohydrate malabsorption. Arq Gastroenterol 1979;16:137–45.
41. Ellstad-Sayed JJ, Levitt MD, Bond JH: Milk intolerance in Manitoba Indian school children. Am J Clin Nutr 1980;33:2198–201.
42. MacLean W, Fink BB: Lactose malabsorption by premature infants: magnitude and clinical significance. J Pediat 1980;97:383–8.
43. Kirchner BS, DeFavaro MV, Jensen W. Lactose malabsorption in children and adolescents with inflammatory bowel disease. Gastroenterology 1981;81:829–832.
44. Unger M, Scrimshaw NS. Comparative tolerance of adults of differing ethnic backgrounds to lactose-containing and lactose-free dairy drinks. Nutr Res 1:227–234, 1981.
45. Kolars JC. Levitt MD, Aouji M, Savaiano D. Yogurt—An autodigesting source of lactose. New Engl J Med 1984:310:1–3.
46. Calloway DH, Murphy EL. The use of expired air to measure intestinal gas formation. Ann NY Acad Sci 1968;150:82–95.
47. Murphy EL, Calloway DH. Effect of antibiotic drugs on the volume and composition of intestinal gas from beans. Am J Dig Dis 1972;17:639–42.
48. Hall RG Jr, Thompson H, Strother A. Effects of orally administered activated charcoal on intestinal gas. Am J Gastroenterol 1981;75:192–6.
49. Hickey CA, Calloway DH, Murphy EL. Intestinal gas production following ingestion of fruits and fruit juices. Am J Dig Dis 1972;17:383–9.
50. Robertson JA, Brydon WG, Tadesse K, et al. The effect of raw carrot on serum lipids and colon function. Am J Clin Nutr 1979;32:1889–92.
51. Tadesse K, Eastwood MA. Metabolism of dietary fibre components in man assessed by breath hydrogen and methane. Br J Nutr 1978;40:393–6.
52. Bond JH, Levitt MD. Effect of dietary fiber in intestinal gas production and small bowel transit time. Am J Clin Nutr 1978;31:S169–74.
53. Anderson IH, Levitt AS, Levitt MD. Incomplete absorption of carbohydrate in all-purpose wheat flour. New Engl J Med 1981;304:891–2.
54. Hollenbeck CB, Coulston AM, Quan R et al. Effects of a commercial starch blocker preparation on carbohydrate digestion and absorption: in vivo and in vitro studies. Am J Clin Nutr 1983;38:498–503.
55. Carlson GL, Li BUK, Bass P, Olsen WA. A bean $\alpha$-amylase inhibitor formulation (starch blocker) is ineffective in man. Science 1983;219:393–5.
56. Stephens AM, Haddad AC, Shillips SF. Passage of carbohydrate into the colon. Direct measurements in humans. Gastroenterology 1983;85:589–95.
57. Church CF, Church HN. Food Values of Portions Commonly Used. 12th Edition. Philadelphia, J.B. Lippincott Co., 1975.
58. Leichter J, Comparison of whole milk and skim milk with aqueous solution in lactose tolerance testing. Am J Clin Nutr 1973;26:393–6.
59. Welsh JD, Manion CV, Griffith WJ, Bird PC. Effect of psyllium hydrophilic mucilloid on oral glucose tolerance and breath hydrogen in postgastectomy patients. Dig Dis Sci 1982;27:7–12.
60. Bond JH, Levitt MD. Fate of soluble carbohydrate in the colon of rats and man. J Clin Invest 1976;57:1158–64.
61. Bond JH, Currier BE, Buchwald H, Levitt MD. Colonic conservation of malabsorbed carbohydrate. Gastroenterology 1980;78:444–7.
62. Ruppin H, Bar-Mair D, Soergel KH, et al. Absorption of short-chain fatty acids by the colon. Gastroenterology 1980;78:1500–7.
63. Saunders DR, Wiggins HS. Conservation of mannitol, lactulose, and raffinose by the human colon. Am J Physiol 1981;241:G397–402.
64. Torún B, Solomons NW, Viteri FE. Lactose malabsorption and lactose intolerance: Implications for general milk consumption. Archivos Latinoamer Nutr 1979;29;445–94.