Use of Pulmonary Hydrogen (H_2) Measurements to Quantitate Carbohydrate Absorption

STUDY OF PARTIALLY GASTRECTOMIZED PATIENTS

JOHN H. BOND, JR., and MICHAEL D. LEVITT

From the University of Minnesota Hospital, Medicine Department, Minneapolis, Minnesota 55455

ABSTRACT A technique was developed to quantitate the absorption of ingested carbohydrate by means of continuous measurements of pulmonary H_2 excretion. This technique is based on the observation that H_2 is produced in the colon when carbohydrate is fermented by colonic bacteria, and this H_2 is then excreted by the lungs. The quantitative relationship of pulmonary H_2 excretion to unabsorbed carbohydrate was studied in nine subjects. After ingestion of 6.5, 13, and 26 g of lactulose (a nonabsorbable disaccharide), H_2 excretion increased linearly, averaging (±1 SEM) 13±3.5, 23±7.2, and 49±7 ml per 2 hr. Because of consistent individual differences in H_2 excretion per gram of lactulose, the variability of this linear response was less in a given subject, with the H_2 excretion after 6.5 g and 26 g lactulose dosages averaging 55±4.2% and 214±16% of that observed after the 13 g dose. It was further demonstrated with fecal homogenates, as well as in rats after direct intracecal instillation of carbohydrate, that there was no significant difference in the rate of H_2 formation from lactulose as compared with the normally ingested sugars. Thus, a subject's H_2 excretion after a 13 g dose of lactulose can be used as a standard to convert H_2 excretion after ingestion of other carbohydrates into grams of carbohydrate not absorbed. Application of this technique to seven partially gastrectomized patients indicated all subjects malabsorbed a portion of a 100 g dose of glucose whereas six of seven completely absorbed a 25 g dose. Malabsorption of physiologic quantities of various carbohydrates was clearly demonstrated in one subject. This technique appears to provide quantitative information on carbohydrate malabsorption not readily obtained by presently available techniques.

Supported by U. S. Public Health Service Grants 5 R01 AM13309, 5 F03 AM42999, M01 RR 400, and University of Minnesota Graduate School Grant 452-0303-4909.

Dr. Bond's present address is the Veterans Administration Hospital, Medicine Department, Minneapolis, Minn.

Received for publication 23 August 1971 and in revised form 27 October 1971.

INTRODUCTION

Understanding of the importance of carbohydrate malabsorption in gastrointestinal disease states is limited by the lack of a quantitative test of carbohydrate absorption comparable to the fecal fat determination used in the study of lipid absorption. Thus, the role of carbohydrate malabsorption in the pathogenesis of diarrhea and malnutrition remains largely speculative in distinct contrast to fat malabsorption which has been studied in a variety of conditions.

Previous experiments indicated that pulmonary H_2 excretion could be used to detect carbohydrate malabsorption (1). This technique is based on the findings that (*a*) H_2 is produced almost entirely in the colon when carbohydrate is fermented by colonic bacteria and (*b*) respiratory H_2 excretion is an accurate indicator of colonic H_2 production (2). Thus, after ingestion of carbohydrate, an increase in breath H_2 excretion occurs only when a portion of the ingested material is not absorbed and delivered to the colonic bacteria.

In the present investigation we first attempted to demonstrate that there is a quantitative relationship between the amount of carbohydrate delivered to the colon and the volume of H_2 excreted. Using this relationship, carbohydrate absorption was measured in a group of patients with diarrhea after subtotal gastrectomy. These studies suggest that H_2 measurements provide quantita-

tive data on carbohydrate absorption which cannot be readily obtained using other available techniques.

METHODS

Subjects. Hydrogen excretion was studied in 17 healthy subjects, 7 patients with subtotal gastrectomies and Billroth II anastomoses, and one patient with bacterial overgrowth of the small bowel secondary to a surgically constructed blind loop. One postgastrectomy patient was asymptomatic while the other six had persistent diarrhea and a variable amount of weight loss after their surgery. Two of these patients who had severe diarrhea and weight loss were hospitalized in the Clinical Research Center and extensively studied. Bacterial culture of the upper jejunum was performed in four of the seven postgastrectomy patients and all had less than 10^6 organisms/ml of jejunal fluid. The patient with bacterial overgrowth of the small bowel had greater than 10^9 organisms/ml of jejunal fluid on three separate occasions.

Measurement of pulmonary excretion rate of H_2. The rate of pulmonary H_2 excretion in human subjects was measured by having the subject breathe for a 3–6 hr period into a closed system somewhat similar to that described by Coburn, Williams, and Kahn (3). The subject sat on a chair and his head was enclosed in a polyvinyl hood which was sealed at the neck with a rubber diaphragm. The gas in the hood was circulated via a pump through a CO_2 absorber, an ice bath, a spirometer, and then back into the hood. Oxygen was added to the system via a solenoid which was activated by a magnetic switch when the spirometer fell to a certain level. The total volume of gas in the system and the lungs (approximately 30 liters) was determined by injecting a known volume of helium at the start of the study and measuring the dilution of this helium 8 min later. This system had a small and variable leak which averaged about 5–10% of the gas volume per hr. This leak rate was determined, and corrected for, by measurement of the decrease in helium concentration which occurred during the experiment. Distribution of helium in body tissue was assumed to be negligible.

The excretion rate of H_2 by rats was determined using a somewhat similar closed-system technique. The rat was placed in a polyvinyl cylinder and the air in the cylinder was circulated through a CO_2 absorber. An O_2 reservoir under 2–3 cm H_2O positive pressure was connected to the cylinder, and O_2 entered the system as CO_2 was absorbed. The gas volume of this system was calculated from the volume (milliliters) of the system when empty minus the weight of the rat in grams.

In each of these closed systems, the quantity of H_2 excreted per unit of time was determined from the volume of gas in the system and the concentration of H_2 present in periodically analyzed samples.

Analysis for H_2 and He. The concentration of H_2 and He was determined by gas chromatography[1] using a thermal conductivity detector. Adequate separation of H_2 and He was obtained on a 9 ft column packed with molecular sieve at an oven temperature of 130°C. Argon was used as the carrier gas at a flow rate of 28 ml/min.

The closed system was connected to a 2 ml gas sampling valve on the gas chromatograph by a polyvinyl tube (3 mm I.D.). When a gas sample was to be analyzed, 100 ml of gas from the system was drawn through the gas sampling valve by means of a 100 ml syringe. After injection of a 2 ml sample into the chromatograph, the 100 ml of gas in the syringe was returned to the closed system.

Measurement of H_2 excretion after carbohydrate ingestion. Subjects were instructed to ingest nothing but water after their evening meal and all studies were carried out on the following morning. In preliminary studies, several base line measurements of H_2 excretion were obtained, the subject then ingested the test sugar, and H_2 excretion was measured for a variable period ranging from 3 to 6 hr. These studies indicated that the base line measurements before carbohydrate ingestion were unnecessary, since in all subjects the base line excretion rate remained unchanged for at least 25 min after ingestion. Therefore, in subsequent studies H_2 measurements were initiated immediately after carbohydrate ingestion.

Lactulose syrup[2] was used to determine the H_2 production which resulted from ingestion of a nonabsorbable carbohydrate. This syrup contains 50 g of lactulose/100 g, and in addition, small and variable quantities of lactose and galactose. In the studies of the quantitative relationship of H_2 excretion to lactulose ingestion, the lactose and galactose were considered to be entirely absorbed, and all H_2 excretion was presumed to result from lactulose malabsorption.

The 5-, 10-, 20-, 50-, and 100-g doses of carbohydrate were given as 50 g/100 ml solutions.

The starch test material consisted of tapioca boiled for 15 min and flavored with cinnamon. The starch concentration was 12 g/100 ml.

Comparison of the rate of H_2 production from various carbohydrates. The rate of production of H_2 from different sugars was studied using fecal homogenates. Fresh fecal specimens (20 g) from 10 subjects were homogenized in 40 ml of 0.10 M phosphate-buffered saline (pH 7.0). 4-ml portions of this homogenate were placed in a series of 10-ml test tubes and 1 ml of 1.25 g/100 ml solution of lactulose, sucrose, glucose, lactose, or maltose was added to the tubes. Pure lactulose[3] rather than the syrup was used in these studies. The tubes were mixed, sealed with rubber stoppers, placed in 37°C water bath, and a needle attached to a 50 ml syringe was inserted through the rubber stopper. At 1 hr, the tubes were vigorously stirred. The gas in each tube was then displaced into the syringe by injection of H_2O into the test tube via a second syringe. The concentration of H_2 in the gas was determined by gas chromatography.

The rate that H_2 was produced in the colon from various carbohydrates was determined in rats. Sprague-Dawley rats weighing 150 g were fasted for 24 hr to reduce base line H_2 production to a low level. Base line measurements of H_2 production were obtained and then, under light ether anesthesia, a small abdominal incision was made, and 1 ml of a 25% solution of lactulose, sucrose, or glucose was instilled via a needle into the cecum. The incision was closed, the animals were allowed to regain consciousness, and the increase in H_2 excretion above baseline levels was determined for a 1 hr period.

RESULTS

Base line H_2 measurements. The base line rate of pulmonary H_2 excretion before carbohydrate ingestion was highly variable and ranged from undectable to 0.23

[1] Beckman GC-5, Beckman Instruments, Inc., Fullerton, Calif.

[2] Philips Roxane, Inc., St. Joseph, Mo.

[3] Philips Roxane, Inc., St. Joseph, Mo.

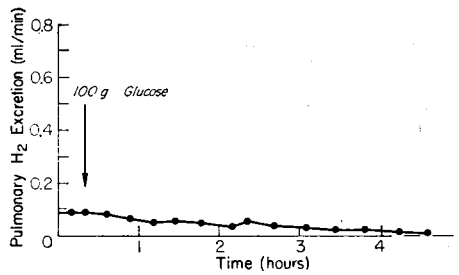

FIGURE 1 Pulmonary H_2 excretion by a healthy subject after ingestion of 100 g of glucose.

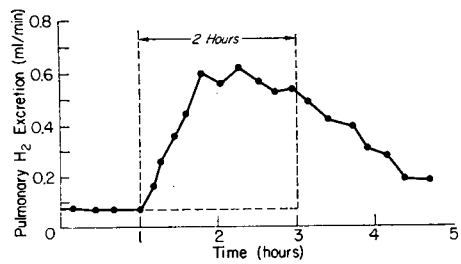

FIGURE 2 Pulmonary H_2 excretion by a healthy subject after ingestion of 26 g of lactulose at zero time.

ml/min. The base line H_2 excretion of the healthy subjects (0.084±0.060 ml/min) did not differ significantly from that of the seven postgastrectomy patients subsequently demonstrated to have carbohydrate malabsorption (0.092±0.084 ml/min).

H_2 excretion of healthy subjects after glucose ingestion. The ingestion of 100 g of glucose by 10 healthy subjects was never associated with an increase in H_2 excretion and usually was followed by a gradual decline in H_2 excretion. Fig. 1 shows the typical pattern of H_2 excretion after glucose ingestion by normal subjects. This falloff in H_2 excretion is also seen in fasting subjects and apparently results from the utilization of carbohydrate present in the colon at the start of the study.

H_2 excretion in healthy subjects after lactulose ingestion. The ingestion of varying doses (6.5 to 26 g) of lactulose, a completely nonabsorbable sugar, by 17 healthy subjects was associated with an abrupt increase in H_2 excretion as typified by the pattern shown in Fig. 2. The increase in H_2 excretion occurred from 27 to 169 min after ingestion of the lactulose which apparently represents differences in small bowel transit time. The peak rate of H_2 production occurred within 2 hr of the onset of the rise in excretion rate and then gradually tailed off over a 6–8 hr period.

In order to determine if there was a quantitative relationship between the amount of H_2 excreted and the quantity of unabsorbed carbohydrate, nine healthy subjects were randomly fed 6.5, 13, and 26 g of lactulose, usually on consecutive days. The quantity of H_2 attributable to malabsorption of the ingested carbohydrate was determined from measurement of the area under the H_2 excretion curve minus the extrapolated base line H_2 production as is shown in Fig. 2. Measurements were originally carried out for a 4 hr period after the increase in H_2 excretion was noted; however, preliminary studies indicated that a 2 hr period after the increase in H_2 production could satisfactorily represent the quantity of H_2 excreted.

In each of the nine subjects, the volume of H_2 excreted over this 2 hr period always increased as the dosage of lactulose was increased. Fig. 3 shows typical H_2 excretion curves for a subject after 6.5-, 13-, and 26-g dosages of lactulose. The mean H_2 excretion after these doses of lactulose showed a linear increase (see Fig. 4*A*) and as demonstrated in Fig. 4*B* an average of about 1.9 ml of H_2 per 2 hr was excreted for each gram of lactulose ingested, independent of the total dosage of lactulose. Because some subjects consistently produced greater or lesser quantities of H_2 per gram of lactulose than did the remainder of the group, the linear relationship between H_2 excretion and lactulose dosage was much better for a given subject than for the group as a whole. When the H_2 response of an individual to the 6.5- and 26-g doses of lactulose was compared to his response to the 13 g dose, the H_2 excretion after the 6.5- and 26-g doses, respectively averaged 55±4.2% (SEM) and 208±16% of that after the 13 g dose. The co-

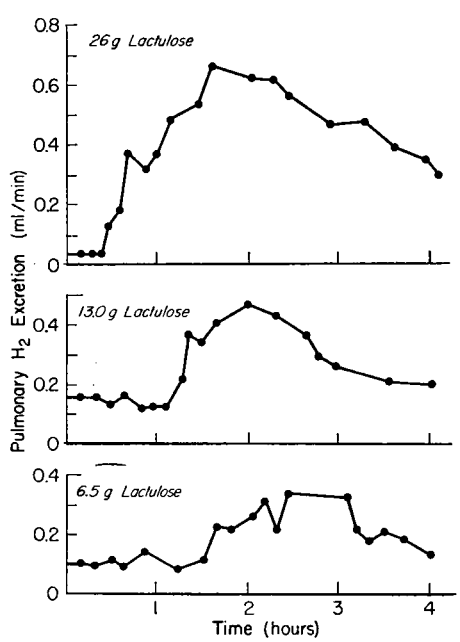

FIGURE 3 Pulmonary H_2 excretion by a healthy subject after ingestion of 26, 13, 6.5 g of lactulose at zero time.

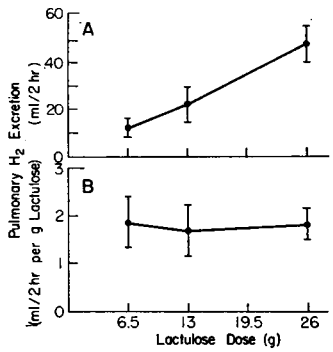

FIGURE 4 (*A*) Pulmonary H_2 excretion (mean ±1 SEM) by nine healthy subjects after ingestion of 6.5, 13, and 26 g of lactulose. (*B*) Pulmonary H_2 excretion (mean ±1 SEM) by nine healthy subjects after ingestion of 6.5, 13, and 26 g of lactulose expressed as milliliters H_2/2 hr per g lactulose ingested.

efficient of variation (SD/mean) of these intra-individual comparisons was less than one-fourth that of the comparable values obtained when data from all subjects were compared.

The reproducibility of the H_2 response of an individual to a 13 g dose of lactulose was studied in four individuals. The results of the repeat study averaged 104% (range 87–111%) of the first study.

Comparison of the rate of H_2 production from lactulose and other carbohydrates. In order to use lactulose as a standard to estimate the malabsorption of other carbohydrates, it must be shown that H_2 is liberated at approximately the same rate from each of these carbohydrates. A comparison was made of the H_2 liberated per hour by fecal homogenates from solutions containing lactulose, glucose, sucrose, lactose, and maltose. Negligible H_2 was produced when no sugar was added to the homogenate. Although there were greater than

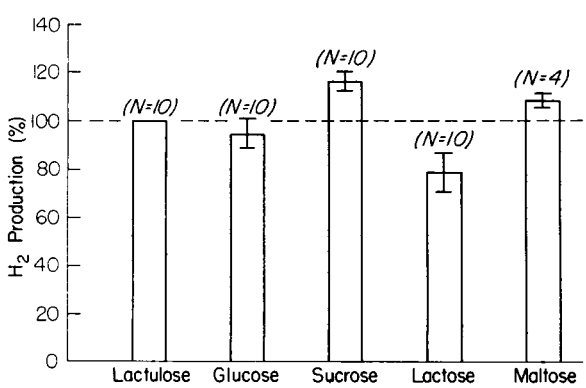

FIGURE 5 H_2 production (mean ±1 SEM) by fecal homogenates after the addition of glucose, sucrose, lactose, and maltose, expressed as a percentage of the hydrogen produced by homogenates after addition of lactulose.

50-fold differences in the rates of H_2 production by different fecal specimens, the production rate by a given specimen was roughly the same for each of the sugars tested. Fig. 5 shows H_2 production for each of the normally ingested sugars expressed as a percentage of the H_2 produced by that specimen during lactulose fermentation. H_2 production from each of these sugars was not significantly different ($P > 0.05$) from that of lactulose. It was possible that the similar amounts of H_2 produced over a 1 hr period merely represented the maximal amount of H_2 that could be produced by a homogenate, and the actual rate of H_2 formation from the different sugars might be highly variable. However, measurements of H_2 production obtained at intervals over the 60 min period with two of the homogenates indicated that the rate of H_2 production from each of the sugars was roughly similar over the entire 60 min period.

The possibility was also investigated that the quantity of H_2 produced in the test tube might not adequately reflect what occurs in the complex environment of the colon. Therefore, H_2 production by rats was determined after intracecal instillation of lactulose, glucose, and sucrose. While there was a marked variability in the quantity of H_2 excreted by different rats, there was no significant difference in the rate of colonic H_2 production from each of these sugars as shown in Fig. 6.

H_2 excretion of patients after ingestion of carbohydrates. Each of the seven patients with a subtotal gastrectomy was fed 13 g of lactulose to determine the standard H_2 response of that individual when 13 g of carbohydrate was not absorbed. Only glucose absorption was studied in five of these subjects. In sharp contrast to the finding in healthy controls, there was a marked increase in H_2 excretion by each subject after ingestion of 100 g of glucose with calculated glucose malabsorptions of 2.9, 13.7, 13.8, 15.2, and 17.2 g, respectively. The subject who malabsorbed only 2.9 g was the only patient who did not have diarrhea after

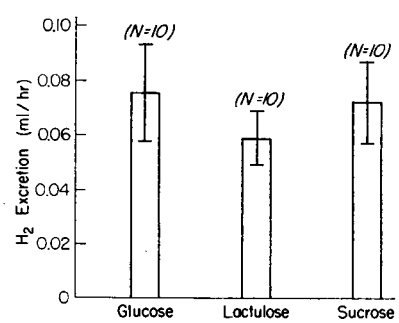

FIGURE 6 H_2 excretion (mean ±1 SEM) by rats after the intracecal instillation of glucose, lactulose, and sucrose.

TABLE I

Absorption of Carbohydrates by Two Patients with Diarrhea after Partial Gastrectomy

Test carbohydrate	Dose	Quantity of carbohydrate not absorbed	
		Patient H. J.	Patient G. T.
	g	g	g
Glucose	50	21	17
	25	4	—
	10	0	—
Maltose	50	15	11
	25	5	—
Sucrose	50	10	0
	25	0	—
Lactose	50	11	6
	25	11	—
Starch	25	15	0
	10	2	—

his subtotal gastrectomy. A 25 g dose of glucose was completely absorbed by all subjects.

The ability of the two subjects (H. J. and G. T.) with severe diarrhea to absorb varying dosages of different sugars and starch is shown in Table I.

H_2 production from starch was not studied in the fecal homogenates nor the rat colon studies. However, it seems likely that due to the action of amylase the bulk of the nonabsorbed starch would probably enter the colon as maltose or be converted to maltose shortly thereafter. Thus, it was assumed that H_2 production from starch would be roughly comparable to that from an equivalent quantity of maltose.

The possibility that appreciable H_2 production might occur in the small intestine if there is bacterial overgrowth was tested in the patient with a blind loop. After a 10 g dose of glucose, a very slight but probably significant increase in H_2 excretion occurred (see Fig. 7) which was equivalent to the malabsorption of 0.66 g of glucose. The H_2 production returned to base line levels within 2 hr of carbohydrate ingestion, a phenomenon never observed after malabsorption of carbohydrate. The small (10 g) dosage of glucose was selected because all postgastrectomy patients previously studied had completely absorbed this dosage and it was therefore anticipated that all H_2 produced would represent production in the small intestine.

DISCUSSION

In the present study, carbohydrate absorption was quantitatively assessed by comparing the volume of H_2 excreted after ingestion of a test sugar with that excreted after ingestion of the nonabsorbable sugar, lactulose. The validity of this technique is based upon the following assumptions: (*a*) lactulose (1-4-β-galactosido-fructose) is not absorbed in the small bowel and is quantitatively delivered to the colon; (*b*) the amount of H_2 produced by the colonic bacteria is directly proportional to the load of lactulose reaching the colon; and (*c*) similar quantities of H_2 are liberated during fermentation of equivalent loads of lactulose and the test sugars.

Evidence that the human small bowel is unable to absorb lactulose is provided by studies demonstrating that lactulose ingestion is not followed by an increase in blood-reducing substances (4) nor by the excretion of lactulose in the urine (5). In addition, the enzyme which hydrolyzes lactulose to its component monosaccharides is not present in human small intestinal mucosa (6).

The assumption that H_2 production is directly proportional to the quantity of lactulose entering the colon is supported by the studies of H_2 excretion of subjects after the ingestion of increasing doses of lactulose shown in Fig. 4. Much of the scatter of the data shown in this figure resulted from subjects who tended consistently to excrete large or small quantities of H_2. Thus, a given individual always showed a relatively good linear relationship between the quantity of lactulose ingested and the volume of H_2 excreted.

The final assumption concerning the volume of H_2 produced during fermentation of various sugars was tested in human fecal homogenates as well as in the colon of the intact rat. In both of these systems, no significant difference was observed in the formation rate of H_2 from lactulose when compared to the formation rate from the commonly ingested sugars. Absolute assurance that H_2 production occurs at the same rate from different sugars in the human colon will require direct intracecal injection of the sugars via intestinal tube.

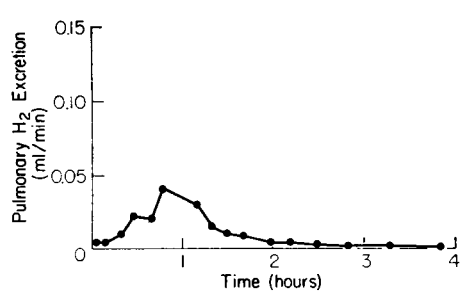

FIGURE 7 Pulmonary hydrogen excretion after the ingestion of 10 g of glucose at zero time by a subject with bacterial contamination of the small intestine.

Possible sources of error using this technique could result from abnormalities of the intestinal flora. Bacterial contamination of the small bowel might result in the production of H_2 in the small intestine, thus simulating malabsorption. However, the one patient with bacterial overgrowth investigated in this study produced only minimal quantities of H_2 in the small bowel. Furthermore, the rapid return to the base line H_2 excretion rate observed in this patient suggests that H_2 produced in the small bowel can be distinguished from H_2 resulting from malabsorption.

It appears certain that the H_2 excretion which followed the ingestion of large doses of carbohydrate by the subtotal gastrectomy patients resulted from malabsorption rather than bacterial overgrowth. First, the jejunal cultures of these patients revealed relatively normal numbers of organisms ($< 10^6$ organisms/ml). Second, no increase in H_2 excretion was noted after ingestion of small doses of carbohydrate (i.e. 25 g of glucose) which would have been expected to yield readily detectable quantities of H_2 if this gas was derived from fermentation in the upper small bowel.

A final source of error is represented by a previously encountered patient whose fecal flora did not produce H_2 during carbohydrate fermentation (1). While this phenomenon is rare, obviously the technique described in this paper is of no value in such subjects.

The accuracy of this technique for measuring carbohydrate absorption can be partially assessed by determining the accuracy with which the 6.5- and the 26-g doses of lactulose could be predicted from the H_2 excretion which followed their ingestion. Using an individual's H_2 excretion after a 13 g dose of lactulose as a standard, the 95% confidence interval for the 6.5 g dose ranged from 3.1 to 9.9 g and for the 26 g dose from 13 to 39 g. If other carbohydrates are fermented at the same rate as lactulose, the malabsorption of these sugars should also be estimated with a 95% confidence interval of about ±50% of the actual quantity malabsorbed.

It is not possible to compare the accuracy of this technique for estimating carbohydrate absorption with that of the quantitative fecal fat determination since the accuracy with which the fecal fat measurements actually reflect the quantity of malabsorbed fat entering the colon has apparently not been investigated.

While the errors involved in the determination of carbohydrate malabsorption by H_2 measurements are admittedly quite large, this method provides data not readily obtainable by other techniques. The clinical assessment of carbohydrate malabsorption is usually limited to the performance of tolerance tests. These tests do not provide a quantitative measure of absorption and they may be influenced by a variety of factors other than intestinal absorption such as gastric emptying and intermediary carbohydrate metabolism. It is apparent from the present study of postgastrectomy patients that massive malabsorption may occur in the face of a normal tolerance test.

An inherent disadvantage of tolerance tests is that they reflect the quantity of carbohydrate absorbed. Therefore, they cannot detect the failure to absorb small fractions of a carbohydrate load. In contrast, H_2 excretion like the fecal fat measurement, reflects the quantity of material not absorbed and thus can detect minimal degrees of malabsorption.

Intestinal perfusion studies provide a precise measure of the absorption rate of a segment of bowel under the controlled condition of the perfusion. However, these studies cannot predict the absorptive capacity of the intestine for ingested carbohydrate loads.

The only presently available method for quantitating the absorption of ingested carbohydrates is the method of Borgstrom, Dahlquist, Lundh, and Sjovall (7) in which terminal ileal aspiration is carried out after ingestion of a mixture of a test substance and a nonabsorbable marker. As discussed by Soergel (8), sizeable errors may result in calculating absorption by this technique. In addition, the possible influence of intestinal intubation on absorptive function has never been investigated. Nevertheless, it appears that comparison of the results of H_2 measurements with those of ileal aspiration represents the only means available to further investigate the validity of the technique described in this paper.

The use of H_2 measurements to assess absorption is painless and the closed system is well tolerated by patients. The measurement of H_2 and He concentrations using gas chromatography is simple and takes only about 3 min.

Drawbacks to the widespread use of this technique include the need for relatively expensive equipment and the time required for each study which consists of about 4 hr to measure the H_2 response to lactulose and a similar amount of time for each test carbohydrate load.

The data obtained in patients with subtotal gastrectomies and diarrhea are presented as a demonstration of the clinical applicability of this technique. Patients with a history of diarrhea after subtotal gastrectomy consistently malabsorbed large quantities of a 100 g dose of glucose. Intestinal mucosal biopsies were normal in three of these patients; thus it seems likely that this malabsorption resulted from rapid deposition of large quantities of a hypertonic solution into the small bowel. Similar findings were obtained by Lundh (9) who sampled mid-ileal contents after ingestion of a meal containing 900 mM of sugar.

It is apparent that the intestine did not absorb a fixed percentage of the glucose load, as is stated to occur with fat (10), since six of the seven patients completely absorbed 25 g of glucose. Rather, there appeared to be a maximal amount of glucose which was completely absorbed and, when this maximum was exceeded, malabsorption occurred.

Lastly, the studies carried out in patient H. J. (Table I) demonstrate that appreciable malabsorption may also occur after ingestion of physiologic quantities of carbohydrate. This malabsorption may play an important, but frequently unrecognized, role in the diarrhea and malnutrition of partially gastrectomized patients.

REFERENCES

1. Levitt, M. D., and R. M. Donaldson. 1970. Use of respiratory hydrogen (H_2) excretion to detect carbohydrate malabsorption. *J. Lab. Clin. Med.* **75**: 937.
2. Levitt, M. D. 1969. Production and excretion of hydrogen gas in man. *N. Engl. J. Med.* **281**: 122.
3. Coburn, R. F., W. J. Williams, and S. B. Kahn. 1966. Endogenous carbon monoxide production in patients with hemolytic anemia. *J. Clin. Invest.* **45**: 460.
4. Hoffman, K., D. A. Mossel, W. Korus, and J. H. van de Kamer. 1964. Untersuchungen über die wirkungsweise der lactulose (β-galactosido-fructose) im darm. *Klin. Wochenschr.* **42**: 126.
5. Muller, M., J. Walker Smith, D. H. Shmerling, H. Curtius, and A. Prader. 1969. Lactulose: a gas-liquid chromatography method of determination and evaluation of its use to assess intestinal mucosal damage. *Clin. Chim. Acta.* **24**: 45.
6. Dahlquist, H., and J. D. Gryboski. 1965. Inability of the human small intestinal lactase to hydrolyze lactulose. *Biochim. Biophys. Acta.* **110**: 635.
7. Borgstrom, B., A. Dahlquist, G. Lundh, and J. Sjovall. 1957. Studies of intestinal digestion and absorption in the human. *J. Clin. Invest.* **36**: 1521.
8. Soergel, K. H. 1968. Inert markers (editorial). *Gastroenterology.* **54**: 449.
9. Lundh, G. 1958. Intestinal digestion and absorption after gastrectomy. *Acta Chir. Scand. Suppl.* 231.
10. Kasper, H. 1970. Faecal fat excretion, diarrhea, and subjective complaints with highly dosed oral fat intake. *Digestion.* **3**: 321.