Interpretation of the breath hydrogen profile obtained after ingesting a solid meal containing unabsorbable carbohydrate

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SUMMARY The extent to which monitoring breath hydrogen excretion provides information concerning the entry of the residues of a solid test meal into the colon was investigated in 89 normal subjects, and 11 patients with the irritable bowel syndrome. The profile of breath hydrogen concentration showed an early peak, that occurred soon after ingesting the test meal in 89% subjects. This was followed by a later more prolonged rise in breath hydrogen concentration. The early peak occurred well before a radioactive marker, incorporated in the test meal, reached the caecum and the data suggest it was predominantly caused by the emptying of the remnants of the previous meal from the ileum into the colon. This hypothesis was supported by direct measurements of the rate of delivery of ileostomy effluent in 12 subjects with terminal ileostomies. Fermentation of carbohydrate in the mouth may, however, contribute to the initial peak, but this contribution may be avoided by collecting gas samples from the nares. The secondary rise in breath hydrogen excretion was closely correlated with the arrival of the radioactive marker in the caecum ($r=0.91$, $p<0.001$), though the time, at which the secondary peak of breath hydrogen excretion occurred was poorly correlated with the time that all the radioactive test meal had entered the colon. When lactulose was infused directly into the colon, as little as 0·5 g produced a discernible hydrogen response, which occurred within two minutes of the infusion. Increasing the rate of colonic infusion of a 50 ml solution of 10% lactulose from 0·02 to 0·15 g/min in five subjects significantly increased the breath hydrogen concentration. At infusion rates below 0·075 g lactulose/minute, the peak breath hydrogen response preceded the end of the infusion, while at higher rates of infusion, the peak hydrogen response occurred after the end of the infusion. Although these results confirmed that monitoring breath hydrogen concentration usefully signalled the time taken for a meal containing unabsorbed carbohydrate to reach the colon, it did not reliably indicate the time when all of the meal had entered the colon. Finally, the use of the maximum increase in breath hydrogen concentration as an index of the degree of carbohydrate malabsorption assumes uniform rates of entry into the colon.

Hydrogen gas is not formed by mammalian cells, but is usually produced in the human colon by the fermentation of unabsorbed carbohydrate by anaerobic bacteria. The gas diffuses rapidly through the colonic epithelium into the blood, is carried to the lungs and is excreted in the breath. Monitoring the breath hydrogen concentration has been used to measure how quickly a drink containing the dis-

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accharide, lactulose, takes to reach the colon[1] and to quantify the malabsorption of lactose or starch by comparing the hydrogen produced after ingesting the test substance with that produced by a known amount of lactulose.[2 3] More recently, technical improvements in breath hydrogen monitors[4] have allowed accurate and sensitive measurements of the small bowel transit time of a meal containing unabsorbable carbohydrate.[5] This paper investigates (a) the extent to which measurements of breath hydrogen concentration can provide an index

of the entry of a solid meal into the human colon, (b) the cause of the initial peak of breath hydrogen, which often begins as the subject eats a meal, and (c) the effect of the rate of entry of a standard amount of carbohydrate into the colon on the increases in breath hydrogen concentration. Studies were carried out after ingesting a standard meal and after infusion of lactulose directly into the colon.

Methods

SUBJECTS
Experiments were conducted in a total of 89 normal healthy volunteers (59 men, 30 women; aged between 19 and 70 years), 11 patients with the irritable bowel syndrome (three men, eight women, aged between 23 and 53 years) and 12 patients (four men, eight women, aged between 28 and 76 years) who had a terminal ileostomy fashioned at least nine months previously for ulcerative colitis. None of the ileostomists had resection of more than six inches of terminal ileum. The patients with the irritable bowel syndrome (IBS) presented with a compatible history of abdominal pain and bowel disturbance and had negative results to an extensive series of screening investigations,[6] which included a ^{14}C-glycocholate breath test to rule out bacterial overgrowth of the small intestine. Each subject gave his or her written informed consent for the tests described below to be carried out, and the protocol was approved by the ethical subcommittee of the Sheffield Area Health Authority on 2 July 1979. Studies involving the ingestion of radioisotopes were carried out in females of the reproductive age range, only if they gave written assurance that to their knowledge they were not pregnant and they were taking adequate contraceptive measures.

MEASUREMENT OF BREATH HYDROGEN PROFILE AFTER INGESTING A SOLID MEAL
Experiments were carried out in 66 normal subjects, who were instructed to avoid ingesting any foods containing unabsorbable carbohydrate (beans, fruit, vegetables, bran, porridge, etc) on the day before the study was carried out. After fasting from 7 pm the previous evening, each subject ingested a solid test meal,[5] consisting of three frankfurter sausages (60 g), 150 g mashed potato, 120 g baked beans, and a dessert of homogenised pineapple sweetened with sucrose and thickened with custard powder (75 g). Sips of water up to a total volume of 50 ml were allowed with the meal. The meal was consumed within seven minutes in every case.

After eating the meal, each subject lay supine on a comfortable bed. Samples of 50 ml end expiratory air were obtained before ingestion of the meal and at 10 minute intervals thereafter until the end of the study, using a modified Haldane Priestley tube.[7] Each sample was injected into a hydrogen detector (GMI, Renfrew, Scotland; and Hansatech, Kings Lynn, England), which contained a gas sensitive polarographic cell[4 8] and yielded a digital read out of hydrogen concentration in parts per million (ppm). The output from the detector was linearly related to breath hydrogen concentration over a range from 0 to 1000 ppm and was able to detect changes of as little as 1 ppm anywhere in that range.[4] The data were then plotted on a graph to yield a profile of breath hydrogen excretion for at least six hours after ingesting the meal.

In a separate series of paired experiments, carried out in eight normal subjects, the effect of food eaten previously on the breath hydrogen profile obtained after ingestion of the test meal was studied. In one experiment, subjects were instructed to eat a meal containing approximately 100 g baked beans as a source of unabsorbable carbohydrate between 9 and 10 pm the previous evening, while in the second they fasted from 6 pm after eating a light meal containing no unabsorbable carbohydrate. The order of the experiments was randomised.

COMPARISON OF THE BREATH HYDROGEN PROFILE WITH THE DELIVERY OF A RADIOLABELLED MEAL TO THE CAECUM
Experiments were carried out in 20 normal subjects and 11 patients with the irritable bowel syndrome. The meal was identical to that described above except that 250 microCuries (9·25 MBq) ^{99m}Tc-sulphur colloid (half life=6 h) were incorporated in the water that reconstituted the mashed potato. The whole body radiation dose from 250 microCuries of ^{99m}Tc-sulphur colloid was less than 5 mrads and the dose to the gonads was less than 20 mrads.

Immediately after ingesting the meal, the subject lay supine on a couch and a gamma camera (Elscint, model 400T, Israel) was positioned approximately 10 cm above the abdomen so that the whole of the abdominal contents could be monitored. The gamma camera was linked to a dedicated minicomputer. Cumulative images of the distribution of radioactivity in the abdominal cavity were recorded every five minutes until the majority of the meal residues appeared to be in the colon. The images were stored on a data processing magnetic disk, for subsequent computer analysis. The position of the colon was identified in the last few images and outlined so that the proportion of the total abdominal counts in the colon could be determined in each 5 minute image.[9] From these data, a profile of colonic filling was constructed and compared with the breath hydrogen profile.

STUDIES CARRIED OUT IN ILEOSTOMISTS

The effect of eating a meal on the expulsion of small intestinal contents from the terminal ileum was investigated in 12 patients with terminal ileostomies.[10] Patients were instructed to have no food after 6pm on the day preceeding the study. At 9.30am on the test day, they ate a solid test meal consisting of 100 g boiled lean ham, 218 g mashed potato (30 g potato powder and 188 ml of deionised water), 100 g washed baked beans (75 g beans plus 25 ml deionised water) and 25 ml corn oil. Fifty micro-Curies of ^{99m}Tc-sulphur colloid were added to the water that reconstituted the mashed potato. The constituents were thoroughly mixed before being eaten, and each subject drank 100 ml water with the meal. All subjects ate the meal within 15 minutes. Patients emptied their ileostomy bag on waking, immediately before ingesting the meal, and subsequently at 30 minute intervals throughout the day until approximately 11pm, and again immediately on waking the following morning. Samples were collected in individually labelled plastic containers and stored in a refrigerator until the study was completed.

Drinks of bland, unsweetened fluids were allowed *ad lib* throughout the day, but no further food was eaten until approximately 6pm, when the patients ate their usual evening meal, labelled with 100 g boiled beetroot as a marker. Each patient was instructed to chew the beetroot thoroughly before swallowing it. This ensured that the marker would be well mixed with the meal. Observations carried out *in vitro* showed that masticated beetroot stained both liquid and solid components of the meal.

On the morning following the test, each ileostomy sample was weighed and the radioactivity counted by inserting the container into the well formed by an inverted collimator and sodium iodide crystal scintillation detector. The radioactive counts were corrected for the volume of the sample.[10] From these data a graph was constructed of the rate of delivery of effluent from the test meal (containing the radioactive marker) throughout the day, marking the time at which the second meal was eaten and the time when the beetroot from the second meal appeared in the bag.

To validate the use of the radioactive marker in these experiments and the studies carried out in normal subjects, the delivery of ^{99m}Tc was compared to the delivery of the components of the meal by analysis of sequential samples of ileostomy effluent in three different subjects. In each case, there were excellent correlations between the delivery of the radioactive isotope and the delivery of absorbable carbohydrate ($r > 0.994$, $p < 0.001$), protein ($r > 0.999$, $p < 0.001$) and fat ($r > 0.975$,

$p < 0.001$).

MEASUREMENT OF THE BREATH HYDROGEN PROFILE AFTER INFUSION OF LACTULOSE DIRECTLY INTO THE COLON

Breath hydrogen excretion was measured after infusion of lactulose into the colon of 18 healthy volunteers. On the day before the study, each subject swallowed a narrow radio-opaque polyvinyl tube, which terminated in a latex balloon containing 1·2 ml elemental mercury. The sealed mercury balloon was connected to the radio-opaque polyvinyl tubing by a short length (4 cm) of slightly wider clear polyvinyl tubing, which fitted snugly over the radio-opaque tubing, but was not glued to it. The subject was screened by fluoroscopy and when the mercury balloon had reached the ligament of Treitz, the proximal end of the tube was attached to a short stiffer polyvinyl tube inserted through the nose into the mouth. Both tubes were then pulled back through the nose and the shorter tube was disconnected. This procedure reduced the discomfort of intubation and enabled the tube to be retained *in situ* for several days. The subject was then allowed to eat, whereupon the tube progressed down the intestine. When the sealed mercury bag had reached the colon, it was blown off the end of the tube by rapid injection of 20ml air and eventually passed in the faeces.

Subjects fasted overnight before the experiment. Then, after brief radiographic screening (<5s) to ensure that the end of the tube was still in the colon, boluses of either 0·5 g or 5 g lactulose (made up in a 10% solution) were injected into the colon or a 50 ml solution containing 5 g lactulose was infused into the colon at rates varying from 0·02 to 0·15 g per min (duration of infusion from 250 to 33 min) using a syringe pump (Braun Unita 1, Melsungen, W Germany). Breath hydrogen concentration was measured before and at minute intervals during and after infusion of lactulose until either the breath hydrogen concentration had returned to the original baseline, or 400 minutes had elapsed, whichever was sooner.

BUCCAL FERMENTATION OF CARBOHYDRATE

To investigate whether oral production of hydrogen gas could influence the breath hydrogen profile, studies were initially carried out in nine healthy volunteers, who had fasted for 12 hours before the experiment. Samples of end expiratory air and air from the buccal cavity were obtained at minute intervals for five minutes before and after swilling the mouth with lactulose (10 ml of a 50% solution). The mouth was then irrigated with a mouthwash containing 1% chlorhexidine (Corsodyl, ICI), and

the tongue and teeth were brushed with toothpaste containing a mouthwash. The lactulose solution was again administered and further breath samples were obtained every minute for at least five minutes. Samples were taken from the oral cavity using a narrow catheter inserted through closed lips and attached to a syringe, while the subject breathed gently through the nose and apposed the back of the tongue to the soft palate making a closed space. To standardise the procedure, subjects were instructed to create the closed buccal chamber for approximately 30 seconds before the sample was taken. To obtain a sample of alveolar air, subjects were instructed to breath out fully through a modified Haldane Priestley tube[7] and a sample of end expiratory air was aspirated with a syringe from the proximal end of the tube near the mouth.

To investigate whether oral production of hydrogen gas had any influence on the breath hydrogen profiles observed after a solid meal, five subjects brushed their teeth and tongue and irrigated the mouth with the chlorhexidine mouthwash eight minutes after starting to eat a solid test meal, when an initial peak in breath hydrogen concentration was being recorded. None of these subjects had cleaned their teeth for at least 24 hours before ingesting the test meal.

Results

BREATH HYDROGEN PROFILES FOLLOWING A SOLID MEAL

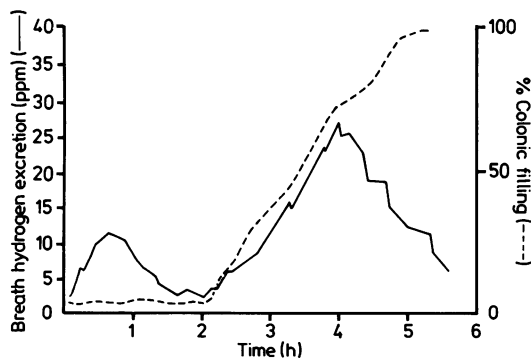Figure 1 shows a typical breath hydrogen profile obtained in a normal subject after ingestion of the solid meal. It consisted of an initial peak of hydrogen, which rose almost immediately after ingestion of the meal and then declined over the next two hours to a baseline, which was less than 10 ppm in all except four subjects. This was followed by a secondary and usually larger rise in breath hydrogen excretion. Breath hydrogen concentration did not return again to the baseline values for at least another six hours. The values characterising the breath hydrogen profile in 66 normal volunteers who ate the same solid meal are shown in the Table.

There was considerable individual variation in the height of the initial peak above preprandial levels (2 to 23 ppm) and the height of the secondary peak above the baseline (5 to 74 ppm).

INITIAL PEAK

Initial peaks were observed in 89% of normal subjects, and were not associated in any study with the appearance of radioactivity in the colon (Fig. 1). The preprandial hydrogen levels, the height of the initial peak and maximum increase above preprandial levels ($10·2\pm2·3$ vs $3·8\pm1·6$ ppm) were significantly higher ($p<0·05$) if normal subjects had eaten a meal rich in unabsorbable carbohydrate the previous evening (Fig. 2).

STUDIES CARRIED OUT IN ILEOSTOMISTS

Ingestion of the test meal was associated in nine out of 12 subjects with an increase in ileostomy output from $1·3\pm0·6$ g/h (mean$\pm$SEM) over the two hour period before ingestion of the test meal to $27·7\pm7·3$ g/h in the hour immediately after ingestion of the test meal ($p<0·001$). In seven patients, this effluent was not labelled with radioisotope and consisted largely of bile stained mucus, but in the remaining two subjects this effluent was radioactively labelled. The mean delivery rate declined in the second hour ($11·7\pm5·6$ g/h) to rise again approximately three hours after ingestion (Fig. 3). This second rise was

Fig. 1 *Relationship between breath hydrogen profile (solid line) and profile of caecal radioactivity (dashed line) after ingestion of a radio-labelled test meal containing baked beans by a normal subject. Biphasic breath hydrogen response is seen. Time from ingestion of meal to secondary rise in breath hydrogen excretion is small bowel transit time.*

Table *The characteristics of profiles in breath hydrogen concentration in 66 normal subjects*

Preprandial levels (ppm)	$8·1\pm8·5$
Initial peak (ppm)	$15·4\pm11·0$
Maximum increase above preprandial levels (ppm)	$7·2\pm4·5$
Duration (min)	114 ± 90
Baseline (ppm)	$4·3\pm6·0$
Secondary peak (ppm)	$26·7\pm14·9$
Increase above baseline (ppm)	$22·5\pm14·2$
Time of secondary rise (min)	
3 ppm increase	240 ± 84
10 ppm increase	303 ± 101
Double baseline	247 ± 84

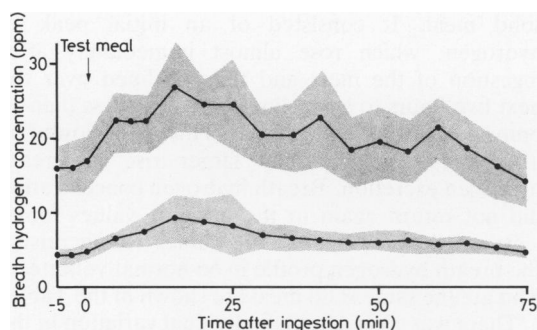Results are expressed as Mean$\pm$SD.

Fig. 2 *Comparison of the average breath hydrogen profiles obtained in eight normal subjects during the initial 75 minutes after ingestion of the solid test meal. Upper profile shows the average (±SEM) response obtained when subjects had eaten a meal, rich in unabsorbed carbohydrate late the previous evening. Lower profile shows the response obtained when the same subjects had eaten a meal, which did not contain unabsorbable carbohydrate, before 6pm on the previous evening.*

associated with an increase in radioactivity and reflected the arrival of the test meal at the stoma.

Ingestion of the second meal was associated with a significant increase (p<0·01) in the delivery of the ileal effluent, that began during the half hour period in which the second meal was eaten (Fig. 3). This was only associated with a small and non-significant increase in radioactivity (Fig. 3). Residues from the second meal, as indicated by the beetroot staining, did not appear in the ileostomy bag until 2·1±1·9 hours (Mean±SD) after starting to ingest the second meal.

EFFECT OF MOUTH FERMENTATION
Swilling the mouth with lactulose produced a significant increase in buccal concentrations of hydrogen (p<0·02) that fell significantly (p<0·02) after the mouth had been irrigated with a mouth-wash and the teeth and tongue brushed with a toothpaste containing a mouthwash (Fig. 4). Corresponding changes in breath hydrogen concentration were observed in samples of end-expiratory air after swilling the mouth with lactulose although these only amounted to 2 ppm and were not statistically significant.

Washing out the mouth with chlorhexidine and brushing the tongue and teeth after ingestion of a standard meal was followed immediately by a transient but non-significant fall in breath hydrogen concentrations during the initial hydrogen peak. This only lasted a few minutes, however, and the hydrogen concentration rose again to reach a maximum value approximately 16 minutes after meal ingestion before declining to a steady baseline.
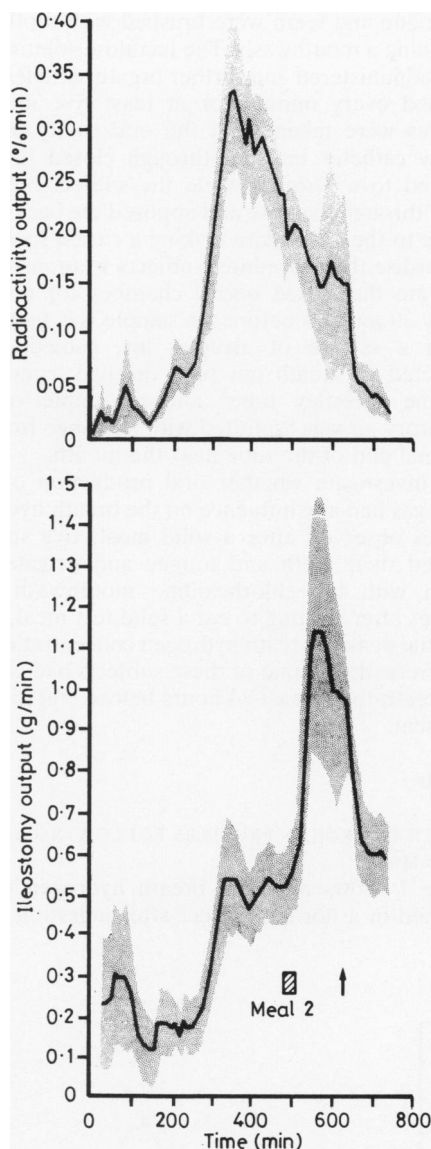

Fig. 3 *Average output of food residues (bottom) and radioactivity (top) in sequential half hour aliquots of ileal effluent voided from terminal ileostomies of 12 patients after ingestion of a radiolabelled, solid test meal. The ingestion of a second meal is indicated by the hatched block and associated with a significant increase in wet weight and a small and non-significant increase in radioactivity. Arrow indicates the average time for appearance of beetroot stained residues.*

SECONDARY RISE
Values for the time of the onset of caecal filling (small bowel transit time of the head of the meal)
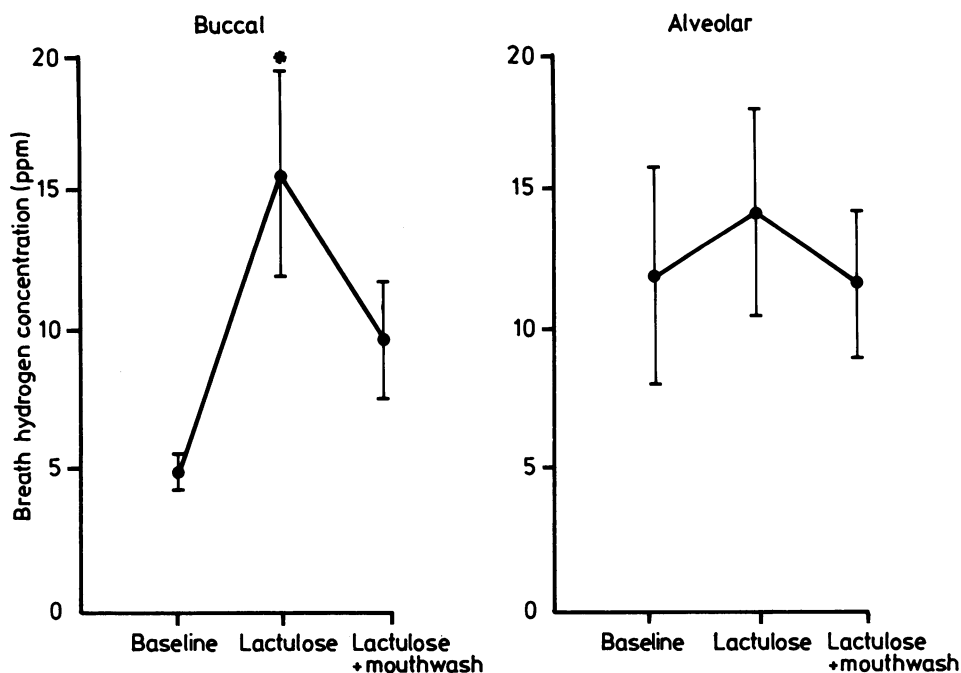
Fig 4. *Effect of swilling the mouth with lactulose, before and after a chlorhexidine mouthwash on hydrogen concentrations in buccal cavity (left) and end expiratory air (right) of nine normal subjects. Asterisk indicates a statistically significant difference between results obtained after swilling the mouth with lactulose and both the baseline results and the results obtained after the use of the mouthwash. Results are expressed as mean±SEM.*

were longer if a rise of 10 ppm above baseline was taken as the index than if a rise of 3 ppm or a doubling of the baseline value was used (p<0·05, Table 1). In 12% of cases (8/66) rises of 10 ppm above baseline were not achieved during this study. Although the average point at which the baseline doubled was not significantly different from the average point at which a rise of 3 ppm occurred, the former depended on the baseline value. If the baseline was lower than 3 ppm, then doubling of the baseline occurred earlier than a rise of 3 ppm (221±17 *vs* 247±19 ppm; p<0·001, n=27), but if the baseline value was above 4 ppm, then doubling of the baseline occurred much later than a rise of 3 ppm (270±17 *vs* 239±17 ppm, p<0·01, n=21).

CORRELATION WITH RADIOACTIVE MEASUREMENTS OF COLONIC FILLING

There was a highly significant correlation (r=0·91, p<0·001) between the time of onset of colonic filling of the radioactive marker in the meal and the time of the secondary increase in breath hydrogen excretion (Fig. 5), defined as an increase in breath hydrogen concentration of 3 ppm above baseline, sustained for at least 30 minutes. In 70% of subjects both

events occurred within 20 minutes of each other. In the remainder, the rise in breath hydrogen concentration occurred after the onset of colonic filling. A similar correlation was obtained when a doubling of the baseline was used as the criterion (r=0·91), but not when a rise in 10 ppm was used (r=0·3, p>0·1). There was no significant correlation between the peak hydrogen excretion and the time at which maximum colonic filling occurred (Fig. 5). In approximately 50% of subjects, peak hydrogen excretion occurred within 20 minutes of the time when all of the radioactive marker appeared to be in the colon. In the remainder, peak hydrogen excretion always occurred before colonic filling of the radioactive marker.

COLONIC INFUSION OF LACTULOSE

Pilot studies carried out in five normal subjects showed that bolus injections of as little as 0·5 g lactulose produced a discernible increase in breath hydrogen concentration of between 5 and 10 ppm occurring within two minutes of ingestion. The period of time over which breath hydrogen concentration remained above the baseline was 173±32 minutes (Mean±SEM; n=5) after a bolus of 5 g
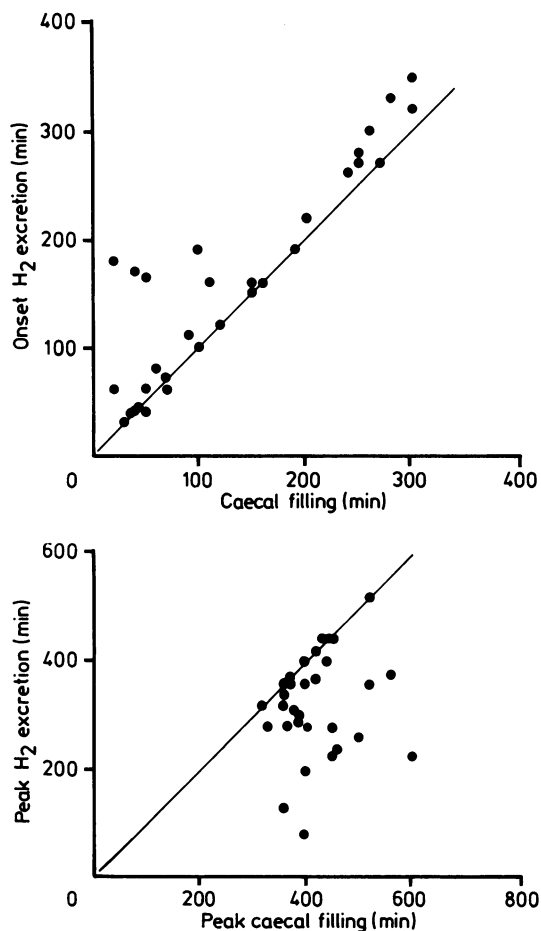
Fig. 5 *Relationship between appearance of radioactivity over caecum and onset of secondary rise in breath hydrogen concentration (top) and between the time that all of the radioactivity had entered the colon and the peak hydrogen concentration (bottom) in 31 subjects (20 normal subjects and 11 patients with the irritable bowel syndrome) after ingestion of a radiolabelled test meal containing baked beans. Lines indicate relationship that would exist if both events occurred simultaneously.*

lactulose had been administered directly into the colon, but was less than five minutes after a 0·5 lactulose bolus.

An increase in breath hydrogen concentration was always recorded within five minutes of the start of infusion of 50ml of a 10% solution of lactulose in all subjects, irrespective of the rate of infusion from 0·02 to 0·15 g lactulose/min. The peak hydrogen concentration occurred after the end of the infusion when the infusion rate was 0·075 g/min or more

rapid in 12 out of 13 experiments. At slower rates of infusion, the peak hydrogen concentration always occurred before the end of infusion (n=7). When half the lactulose was infused at 0·075 g/min and the rest at 0·02 g/min in two subjects, the peak hydrogen concentration was recorded at 106 and 116 minutes before the end of the infusion.

The maximum breath hydrogen concentration showed considerable variation among different subjects even when lactulose was infused at the same rate. For example, in five normal subjects receiving lactulose infusion at 0·15 g/min the maximum increase in breath hydrogen concentration above basal values ranged between 33 and 90 ppm.

When a 50 ml solution containing 5 g of lactulose was infused at different rates in the same five subjects, fast infusion at 0·15 g per minute produced much higher hydrogen concentrations than a slower infusion at 0·02 g per minute (height above basal = 45±10 *vs* 20±3 ppm; p<0·05) (Fig. 6).

Discussion

An increase in breath hydrogen concentration in a normal subject after ingesting a meal is thought to indicate the entry of unabsorbed carbohydrate from the ileum into the pool of colonic bacteria.[1] The typical breath hydrogen profile after ingesting a solid meal consisted of an early initial peak, declining to a baseline and followed some hours later by a secondary more prolonged increase in breath hydrogen excretion.

INITIAL PEAK
The observation that the initial peak in hydrogen concentration was not associated with a concomitant increase in radioactivity over the ascending colon after ingestion of the radiolabelled test meal
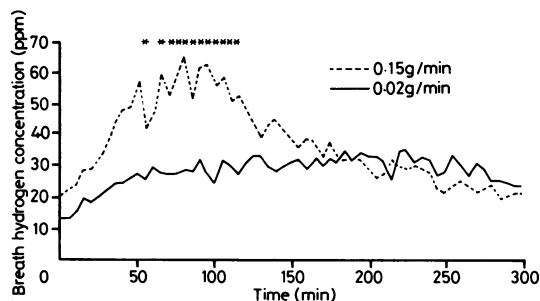

Fig. 6 *The average breath hydrogen profiles recorded in five normal volunteers during colonic infusion of 50 ml of 10% lactulose at 0·02 g/min (bottom) and 0·15 g/min (top). Asterisks indicate a significant difference between results obtained at the times indicated (p<0·05).*

indicated that it was not caused by the rapid transit of the test meal to the colon. An alternative explanation that the initial peak is produced by fermentation of the carbohydrate in the meal by bacteria in the mouth,[11] was supported by the observation that the presence of food or sugar solution in the mouth produced a small peak in breath hydrogen concentration, which was abolished by irrigating the mouth with chlorhexidine solution.[11] While our data have confirmed these observations, it seems unlikely that buccal fermentation is the major cause of the initial hydrogen peak for several reasons; (i) the increase in the end-expiratory or alveolar hydrogen concentration obtained after swilling the mouth with lactulose (2±1 ppm; Mean±SEM) was not statistically significant and was less than the initial peak in alveolar hydrogen concentration observed in normal subjects after ingesting the test meal (7·2±0·6 ppm; p<0·01); (ii) the initial breath hydrogen peak which occurred after ingestion of a meal was not abolished by chlorhexidine; (iii) the initial peak occurred on average 15 minutes after meal ingestion, whereas irrigation of the mouth with lactulose produced a rapid rise in buccal hydrogen within a minute. For future work, contamination of end-expiratory breath samples by buccal fermentation may be avoided by collecting samples from the nose.

The observation that the initial peak was much larger if the subject had eaten a meal containing unabsorbable carbohydrate late on the previous evening suggests that it may have been caused by the entry into the colon of carbohydrate residues, present in the ileum from the previous meal, a manifestation of the so-called 'gastro-ileal reflex'.[12][13] In support of this hypothesis, we found that feeding a meal to ileostomists either increased the rate of emptying of the remnants of the previous meal from the ileostomy, or caused the discharge of bile stained mucus if the last meal had been eaten over 12 hours previously. Although our normal subjects were instructed to avoid foods containing unabsorbable carbohydrate on the day before the test, a certain proportion of starch escapes absorption and may be fermented in the colon,[14] and endogenous mucopolysaccharide can also be a substrate for hydrogen production by colonic bacteria.[15]

SECONDARY RISE

The close relationship between the onset of the secondary rise in breath hydrogen excretion, and the increase in caecal radioacitivy, observed in most of our subjects, confirms the value of breath hydrogen analysis as a method for measuring small bowel transit time of the head of a meal.[5] We found that a rise above baseline of 3 ppm sustained over at least three consecutive readings provided the most reliable index of the arrival of unabsorbed carbohydrate at the caecum. A rise in 10 ppm, if it occurred at all, did not do so until much later and was not significantly correlated with the increase in caecal radioactivity. A doubling of the baseline value, gave similar average results and a similar correlation with caecal radioactivity but individual measurements of transit time using this criterion depended on the height of the original baseline. These comments, can only be taken to apply to our solid meal; a rise of 10 ppm or doubling of the baseline may provide perfectly adequate indices of small bowel transit time of a drink of lactulose.

The sensitivity and accuracy of breath hydrogen analysis as a method for determining the arrival of a meal containing unabsorbable carbohydrate at the caecum was shown by our observations that colonic infusion of lactulose at rates from 0·02 g/min to 0·15 g /min increased the breath hydrogen concentration within five minutes of starting the infusion in 13 out of 14 subjects (when as little as 0·1 g of lactulose had entered the colon), while a bolus of 0·5 g increased breath hydrogen concentration within two minutes. These data confirm and extend previous studies,[1] which showed that direct injections of 5 g lactulose into the caecum of two subjects produced a rise of hydrogen within four and five minutes respectively. The same workers also showed that the small bowel transit time of a drink of lactulose, measured by breath hydrogen excretion, correlated closely with the arrival of a non-absorbable marker (PEG) in the distal ileum (r=0·97).[1]

In view of the above observations, it seems more likely that the occurrence of an increase in caecal radioactivity before the rise of breath hydrogen concentration in 30% patients is probably caused by the presence of radioactivity in loops of ileum overlapping or lying adjacent to the colon. It is unlikely that the discrepancy was caused by the radioactive marker and the unabsorbable carbohydrate reaching the colon at different times, because we showed that the delivery from the terminal ileum of the same radioactive marker incorporated in mashed potato provided an excellent index of the delivery of the protein, carbohydrate and fat components of a similar solid test meal.

The time that the maximum breath hydrogen concentration occurred after ingestion of a meal preceded the time for all of the radioactive marker in the meal to enter the colon in 50% subjects and thus cannot be used as a reliable index of the small bowel transit time of all of the meal. This was confirmed by direct infusion of lactulose into the colon; peak hydrogen excretion occurred well be-

fore the end of the infusion when constant infusion rates were lower than 0·075 g/min, or when the rate of infusion was slowed during the study. On the basis of the colonic infusion studies, we should only expect peak hydrogen excretion to occur at the same time as the entry of all of the food residues into the colon if the rate of entry of unabsorbed carbohydrate is relatively rapid and lies between 0·075 g and 0·15 g/min. This probably explains why we observed a close relationship between peak hydrogen excretion and maximum caecal radioactivity in our previous study, as that included data from studies in which the rate of carbohydrate entry to the colon was accelerated by administration of lactulose.[5]

Previous studies[2] have shown similar rates of hydrogen production when equivalent amounts of different sugars were added to samples of the same faecal homogenate. Comparable results have also been obtained after intracaecal administration of different sugars in rats.[2] These data suggest that it is possible to obtain a quantitative index of the malabsorption of carbohydrate by comparing the breath hydrogen response to ingestion of the test carbohydrate to the response to ingestion of a known amount of unabsorbable lactulose.[2 3 15] In support of this hypothesis, we have previously found that ingestion of meals containing increasing amounts of unavailable carbohydrate produced increasing concentrations of hydrogen in the breath.[5] Our present results showed, however, that the increase in breath hydrogen concentration was much greater if the same amount of lactulose (5 g) was infused into the colon at 0·15 g per minute compared with a slower infusion rate of 0·02 g per minute. Thus estimates of the degree of carbohydrate malabsorption on the basis of breath hydrogen concentration can only be correct if one assumes that the rate of entry of unknown carbohydrate and lactulose are equivalent. This conclusion may not necessarily apply to quantitative measurements of total hydrogen excretion.[2 3]

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