

Bacterial fermentation of fructooligosaccharides and resistant starch in patients with an ileal pouch-anal anastomosis¹⁻³

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ABSTRACT Patients with large bowel disease may undergo ileal pouch-anal anastomosis, in which the colon is removed and part of the distal ileum is used to construct a pelvic reservoir. Competence of the ileal pouch to ferment carbohydrates is associated with the absence of pouchitis. However, the extent to which bacterial fermentation takes place and whether it is affected by diet are unclear. We investigated fermentation of two nondigestible carbohydrates, fructooligosaccharides and resistant starch, in 15 healthy patients with an ileal pouch by using a placebo-controlled crossover design (with glucose as the placebo). Apparent fermentability of fructooligosaccharides was 83%; that of resistant starch was 46%. Resistant starch increased fecal excretion of butyrate by 69% whereas fructooligosaccharides reduced excretion of amino acid-derived isobutyrate by 94% and of isovalerate by 77%. Fructooligosaccharides also significantly increased fecal weight (651 compared with 541 g/d) and breath-hydrogen excretion (286 compared with 85 ppm × h). Bacterial fermentation of nondigestible carbohydrates in pouches takes place to an appreciable extent and in a substrate-specific manner. The relation between such fermentation and inflammation of the pouch (pouchitis) deserves study. *Am J Clin Nutr* 1997;66:1286-92.

KEY WORDS Fructooligosaccharides, resistant starch, ileal pouch-anal anastomosis, fermentation, breath hydrogen, short-chain fatty acids, butyrate, pouchitis

INTRODUCTION

Excision of the colon followed by ileal pouch-anal anastomosis has become a frequently used surgical alternative to permanent ileostomy in patients with ulcerative colitis or familial adenomatous polyposis. In this operation, part of the distal ileum is used to construct a reservoir or pouch that is connected to the anus and provides a measure of continence.

In the months or years after surgery, the pouch gradually acquires a bacterial content and mucosal morphologic characteristics that indicate that the pouch has taken over some colonic functions. Morphologic adaptation of the ileal tissue of the pouch often results in transformation to colonic-type mucosa (1-3). Stasis of the luminal contents in the pouch probably promotes colonization by bacteria. Pouch effluent contains more anaerobic bacteria than does ileostomy effluent (4, 5). Several studies showed considerable excretion of fecal short-

chain fatty acids in pouch effluent (4, 6-9) and, in one study, breath-hydrogen response after consumption of the synthetic disaccharide lactulose was observed in half of the patients (10). Short-chain fatty acids and hydrogen are both end products of fermentation and thus indicate the presence of an active bacterial mass in an ileal pouch.

In healthy humans, fermentation depends to a high degree on composition of the diet and availability of substrates to intestinal microflora (11). However, little or nothing is known about the fate of nondigestible dietary compounds in an ileal pouch and the extent to which bacterial fermentation takes place.

We therefore studied fermentation of two carbohydrates that are not digested or absorbed in the small intestine: fructooligosaccharides and resistant starch. We provided these carbohydrates as supplements to diets of patients with an ileal pouch-anal anastomosis. Fructooligosaccharides occur naturally in, for example, onions and leeks (12-14). We used a native resistant starch that is enclosed in granules such as those in raw potatoes or unripe bananas (15). *In vitro* studies showed that the end products of fermentation of fructooligosaccharides are gases, such as hydrogen, and short-chain fatty acids, mainly acetate (16). Resistant starch is a good substrate for production of butyrate (16), the major fuel of colonic mucosa. In healthy humans, fructooligosaccharides are fermented rapidly whereas resistant starch has a slow, prolonged fermentation (17-19). Thus, these two carbohydrates span the range of fermentability in subjects with a normal gastrointestinal tract, which makes them suitable for examining the extent to which fermentation takes place in patients with an ileal pouch.

The following hypotheses were tested: 1) fructooligosaccharides are fermented more extensively than is resistant starch, as

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reflected in recovery of fructooligosaccharides and resistant starch in pouch effluent; 2) fructooligosaccharides increase breath-hydrogen excretion and total fecal excretion of short-chain fatty acids, especially acetate, and decrease excretion of amino acid-derived short-chain fatty acids; and 3) resistant starch increases breath-hydrogen excretion and total fecal excretion of short-chain fatty acids, especially butyrate.

SUBJECTS AND METHODS

Subjects and experimental design

We recruited 16 patients (8 men and 8 women) who had undergone ileal pouch-anal anastomosis because of ulcerative colitis ($n = 15$) or familial polyposis ($n = 1$). Time since the operation was ≥ 12 mo. The patients had never had clinical signs of pouchitis and were not treated with antibiotics for ≥ 3 mo before the experiment. Subjects were asked to maintain their habitual medication regimen (strictly the same quantities) during the experiment. Five subjects took loperamide (4–16 mg/d) throughout the study; one subject also took prednisone (10 mg/d) and metformin (1500 mg/d). Two subjects smoked and one consumed a lactose-free diet. No subjects were vegetarian.

The study protocol was approved by the Ethical Committee of the University Hospital St Radboud, Nijmegen, Netherlands. All subjects gave informed written consent before participating. After completing the study, patients received a small financial reward, the amount of which was based on the time they had spent in the experiment.

The study was a single-blinded, completely balanced, three-period crossover trial with supplement periods of 7 d separated by 7-d washout periods. Each volunteer took each of the three different supplements in random order. Fecal and breath samples were collected at the end of each supplement period. Subjects kept a diary in which they recorded stool frequency, possible diseases or discomfort, medications used, and deviations in eating, drinking, and lifestyle behavior.

Supplements and food intake

Subjects were asked not to eat probiotic dairy products, which contain microorganisms able to survive passage through the upper gastrointestinal tract, or foods containing large amounts of fructooligosaccharides or resistant starch, such as beans, leeks, and onions. Subjects were given a list of these foods. Participants recorded their habitual diet for 2 d in every supplement period. These food records were coded and nutrient and energy intakes were calculated with use of a modified version of the 1993 Netherlands Nutrient Data Bank (20).

Composition of the supplements is shown in **Table 1**. Subjects consumed half of each supplement at breakfast and the other half at dinner. Supplements were mixed with yogurt, pudding, or orange juice; no change in vehicle was allowed during the experiment. All supplements provided a total of 25.8 g carbohydrate/d. The fructooligosaccharide and resistant-starch supplements each contained 14.3 g nondigestible carbohydrate; the remainder was either digestible or readily absorbable.

Breath samples

On the final day of each supplement period, subjects collected end-expiratory breath samples at 2- or 3-h intervals from

TABLE 1
Composition of dietary supplements

Supplement	Treatment		
	Placebo	Fructooligosaccharides	Resistant starch
Fructooligosaccharides ¹	—	14.3	—
Resistant starch ²	—	—	14.3
Digestible carbohydrates ³	—	0.7	11.5
Added glucose ⁴	25.8	10.8	—

¹ Raftilose P95; Orafiti, Tienen, Belgium; contains 95% oligosaccharides by weight measured by the method described in this paper.

² Hylon VII; Natural Starch and Chemical Company, Bridgewater NJ; contains 55.4% resistant starch by weight measured in vitro according to the method of Englyst et al (15).

³ Other carbohydrates in Raftilose P95 and Hylon VII were mainly glucose, fructose, sucrose, and digestible starch.

⁴ Glucose Pur 01934; Cerestar Benelux BV, Sas van Gent, Netherlands.

0800 (before eating) to 2200 and again at 0800 (before eating) the next morning. They used plastic 60-mL syringes (Sherwood, Ballymoney, Ireland) that were sealed and stored at 4 °C immediately after the sampling. Contents of the syringes were analyzed for hydrogen concentration by using a standard electrochemical cell (Lactoscreen; Hoekloos, Amsterdam) within 24 h after the first sample was obtained. The cell was calibrated with a standard containing 100 ppm H₂ in air (AGA Gas BV, Amsterdam). Twenty-four-hour integrated breath-hydrogen excretion was estimated by calculating geometrically the area under the curve of concentration in relation to time (21).

Stool collection and fecal analyses

On the last day of each supplement period, subjects collected feces for 24 h and stored each stool immediately on dry ice. We collected stools at subjects' homes and stored them at -20 °C. Feces were thawed overnight at 4 °C, weighed, pooled, and homogenized by using a bowl and mixer. The proportion of fecal dry material was estimated by freeze-drying aliquots in triplicate. Another aliquot was ultracentrifuged at 30 000 × *g* for 120 min at 4 °C for preparation of the aqueous fraction of stool. Fecal water was pipetted off and filtered through a 5- μ m filter (Schleicher & Schuell, Dassel, Germany). The pH of the fecal water was determined and samples were stored at -20 °C.

Concentrations of short-chain fatty acids in fecal water were measured in duplicate as described by Tangerman et al (22) by using a gas chromatograph (model CP 9001; Chrompack, Middelburg, Netherlands) and a column packed with 10% SP1200 silicone stationary phase and 1% H₃PO₄ on an 80–100 Chromosorb W acid-washed instrument (Chrompack). An internal standard was added to all samples before analysis (15 mmol 2-ethylbutyric acid/L in 100% formic acid). Fecal excretion of short-chain fatty acids was calculated as fecal weight × proportion of fecal wet material × concentration of short-chain fatty acids in fecal water. In this calculation, the proportion of fecal wet material was defined as 1 minus the proportion of fecal dry material.

Fructooligosaccharides in feces were measured in duplicate samples of 125 mg freeze-dried feces resuspended in 2.4 mL distilled water. D-galacturonic acid (100 [μ]L, 0.5% wt:vol)

was added as an internal standard before extraction. The mixture was vortexed and heated for 15 min at 100 °C and then centrifuged at $13\,000 \times g$ for 30 min. The supernate was analyzed by high-performance anion-exchange chromatography (Dionex BV, Breda, Netherlands) by using a programmable pulse electrochemical detector, a CarboPack PA-100 analytic column (4×250 mm, Dionex), and a mobile phase consisting of 0.1 mol NaOH/L (A) and 1 mol $\text{CH}_3\text{COONa} \cdot 3\text{H}_2\text{O}$ /L containing 0.1 mol NaOH/L (B). A linear gradient was used from 100% A to 70% A plus 30% B in 25 min with a flow rate of 1 mL/min. A calibration curve was made with purified isokestose, which is one of the oligomers in the fructooligosaccharide supplement used in the study. Quantification of fructooligosaccharides in feces was based on this curve and a correction factor was obtained by comparing a known quantity of fructooligosaccharides with the calculated value.

Total starch in stools was determined by subtracting the amount of free glucose from the total amount of glucose obtained after incubation with a starch-degrading enzyme. This method was a modification of that of Björck et al (23). Fifty milligrams freeze-dried feces was suspended in 2 mL water and heated for 5 min at 100 °C; free glucose was then measured with a test kit (catalog no. 716251; Boehringer Mannheim, Mannheim, Germany). For analysis of total glucose, defined as the sum of starch and free glucose, 50 mg freeze-dried feces was suspended in 1 mL water and 1 mL of a solution containing 4 mol KOH/L and incubated for 30 min at room temperature. The suspension was neutralized with hydrochloric acid and diluted (1:1) with 0.4 mol $\text{CH}_3\text{COONa} \cdot 3\text{H}_2\text{O}$ buffer/L (pH 4.75). The mixture was incubated with 20 μL amyloglucosidase (1.4×10^5 U/L; Boehringer Mannheim) for 30 min at 60 °C to hydrolyze the starch and centrifuged for 15 min at $1000 \times g$. Glucose in the supernate was determined by using the test kit. The amount of starch was calculated as the difference between total and free glucose. Mean recovery of starch if added to fecal samples before treatment was 102%. The CV between separately treated and measured duplicates was 8%.

Data analysis

Results are expressed as means \pm SEs unless stated otherwise. The distribution of individual differences was checked for normality by visual inspection of the normal probability plots (univariate procedure; SAS Institute Inc, Cary, NC). The significance of the differences between treatments was assessed by analysis of variance without interactions by using a model with subject and supplement (general linear models procedure). Adding period to this model did not contribute to the significance; thus, there were no significant effects of time or sequence. If there was a significant difference between treatments ($P < 0.05$), group means were compared by using the Tukey test if the model was orthogonal or the Scheffé test if there were missing values in the data set (general linear models procedure). Conventional Pearson's correlation coefficients (correlation procedure) were used to assess relations between dependent variables.

RESULTS

Characteristics of subjects who completed the study and dietary intakes during the study are given in Table 2. One

TABLE 2

Patient characteristics and background diets¹

	Men (n = 7)	Women (n = 8)
Characteristics		
Age (y)	35.6 \pm 6.5	36.5 \pm 7.8
Height (m)	1.80 \pm 0.1	1.66 \pm 0.1
Weight (kg)	80.9 \pm 10.4	66.4 \pm 10.2
Body mass index (kg/m ²)	25.0 \pm 3.0	24.1 \pm 4.1
Diet ²		
Energy (MJ/d)	12.1 \pm 1.3	8.9 \pm 0.6
Carbohydrate (% of energy)	45.1 \pm 4.3	44.0 \pm 6.0
Fat (% of energy)	37.1 \pm 4.3	37.9 \pm 4.7
Protein (% of energy)	15.0 \pm 2.4	17.9 \pm 3.6
Dietary fiber intake (g/d)	20.0 \pm 6.6	13.5 \pm 7.3

¹ $\bar{x} \pm$ SD.

² Supplements not included; maximal contribution of supplements to energy intake was 0.45 MJ/d.

subject withdrew at the end of the first washout period because of endoscopically confirmed pouchitis; data from this subject were excluded from analyses. One subject did not complete the third supplement (fructooligosaccharide) period because of gastrointestinal problems such as vomiting. For this subject, we excluded only data from the fructooligosaccharide period from analyses. All other subjects completed the study without illness. Most subjects had flatulence during fructooligosaccharide supplementation; no other gastrointestinal problems were reported. There were no reports of problems with palatability of the supplements. The food records showed no changes in average daily intakes of energy, protein, fat, carbohydrate, or dietary fiber between treatments.

Bowel habits and stool composition

Data on bowel habits, fecal weight, fecal pH, and fecal excretion of fructooligosaccharides and resistant starch are given in Table 3. There was no fecal excretion of fructooligosaccharides in any subject taking placebo. During fructooligosaccharide supplementation, mean excretion was 2.4 g/d (95% CI: 1.1, 3.7) or 17% of the supplement dose. All constituents of the fructooligosaccharide supplement were present in feces; thus, no selective breakdown of specific oligomers was observed. Fecal excretion of starch was 7.7 g higher per day while subjects were taking the resistant-starch supplement than when they were taking placebo (95% CI: 5.1, 10.4). Because 14.3 g resistant starch/d was added to the diet, 46% of dietary resistant starch was broken down in the alimentary tract.

Fructooligosaccharide supplement increased mean stool frequency by 9% and fecal weight by 20%, or 110 g/d. Percentage of dry matter was not affected by fructooligosaccharides but fecal excretion of dry matter increased by 28.8 g/d (95% CI: 9.5, 48.1; $P = 0.0009$). In subjects taking resistant starch, values for mean stool frequency, fecal weight, and fecal dry matter all tended to be slightly higher than placebo values but the differences were not significant. Fecal water pH tended to be lower (although not significantly) in subjects taking fructooligosaccharides (95% CI: -0.4 , 0.1 pH units) or resistant starch (95% CI: -0.4 , 0.1 pH units) than in those taking placebo.

TABLE 3
Bowel habits, fecal weight, fecal pH, and fecal excretion of fructooligosaccharides and resistant starch after supplementation¹

	Treatment		
	Placebo	Fructooligosaccharides	Resistant starch
Stools per day	6.4 ± 0.6	7.0 ± 0.5 ²	6.8 ± 0.5
Fecal dry matter (%)	12.5 ± 0.5	14.2 ± 0.7	13.4 ± 0.5
Fecal weight (g/d)	541 ± 60	651 ± 67 ³	587 ± 57
Fecal pH ⁴	6.0 ± 0.2	5.8 ± 0.1	5.9 ± 0.1
Fecal excretion			
Starch (g/d)	4.8 ± 0.7	—	12.6 ± 1.3 ⁵
Fructooligosaccharides (g/d)	0 ± 0	2.4 ± 0.6 ³	—

¹ $\bar{x} \pm \text{SEM}$; $n = 15$, except for fructooligosaccharides, for which $n = 14$.
^{2,3,5} Significantly different from placebo: ² $P < 0.05$, ³ $P < 0.01$, ⁵ $P < 0.0001$.
⁴ In fecal water.

Short-chain fatty acids

Fecal excretion of various short-chain fatty acids during the three treatments is shown in **Table 4**. Total amount of short-chain fatty acids excreted tended to be somewhat, although not significantly, higher during supplementation with fructooligosaccharides (95% CI: -3.4, 7.6 mmol/d) or resistant starch (95% CI: -0.1, 10.7 mmol/d) than with placebo. During supplementation with resistant starch, excretion of butyrate was elevated by 69% ($P = 0.0014$). Isobutyrate excretion was lowered by 94% ($P = 0.0006$) and isovalerate excretion by 77% ($P = 0.0023$) during fructooligosaccharide supplementation. We detected no caproate in any of the fecal samples. There was a negative correlation between number of stools per day and total excretion of amino acid-derived short-chain fatty acids ($r = -0.36$, $P < 0.05$).

Breath hydrogen

Breath-hydrogen curves over the last 24 h of each supplement period are shown in **Figure 1**. Integrated breath-hydrogen excretion expressed as area under the hydrogen-time curve was higher during fructooligosaccharide supplementation ($286 \pm 84 \text{ ppm} \times \text{h}$) than during placebo consumption ($85 \pm 17 \text{ ppm} \times \text{h}$; $P = 0.004$). Hydrogen excretion during resistant-starch supplementation was elevated by $125 \text{ ppm} \times \text{h}$ (95% CI: -23.0, 273.4) but the difference with placebo was not significant ($P = 0.046$) when the significance limit was corrected for

TABLE 4
Fecal excretion of short-chain fatty acids after supplementation¹

	Treatment		
	Placebo	Fructooligosaccharides	Resistant starch
	<i>mmol/d</i>		
Total	28.8 ± 3.0	30.9 ± 3.5	34.1 ± 3.2
Acetate (2-carbon)	22.8 ± 2.3	25.2 ± 2.8	26.7 ± 9.16
Propionate (3-carbon)	3.6 ± 0.8	2.8 ± 0.9	3.4 ± 0.8
Butyrate (4-carbon)	2.3 ± 0.4	2.9 ± 1.8	3.9 ± 0.6 ²
Isobutyrate (4-carbon)	0.052 ± 0.02	0.003 ± 0.00 ²	0.022 ± 0.01
Valerate (5-carbon)	0.034 ± 0.02	0.008 ± 0.00	0.010 ± 0.01
Isovalerate (5-carbon)	0.061 ± 0.02	0.014 ± 0.01 ²	0.030 ± 0.01

¹ $\bar{x} \pm \text{SEM}$; $n = 15$, except for fructooligosaccharides, for which $n = 14$.
² Significantly different from placebo, $P < 0.01$.

multiple comparisons. There was no correlation between individual values for integrated breath-hydrogen excretion and fecal excretion of fructooligosaccharides ($r = -0.14$, $P = 0.46$) or resistant starch ($r = -0.09$, $P = 0.64$).

DISCUSSION

We found that fructooligosaccharides and resistant starch, two nondigestible carbohydrates commonly found in foods, are well fermented in patients with an ileal pouch-anal anastomosis. To our knowledge, this was the first quantitative study of carbohydrate fermentation in this patient group.

Apparent fermentability of fructooligosaccharides and resistant starch

Mean recovery of fructooligosaccharides in feces was 17% of the daily dose of supplement. Fructooligosaccharides are not metabolized by human digestive enzymes and most fructooligosaccharide molecules survive passage through the upper part of the gastrointestinal tract (24-28). It is thus likely that most fructooligosaccharides in our study were fermented by bacteria in the ileum or pouch. No fructooligosaccharides were recovered from feces of any subject taking placebo, probably because of low amounts of fructooligosaccharides in the back-

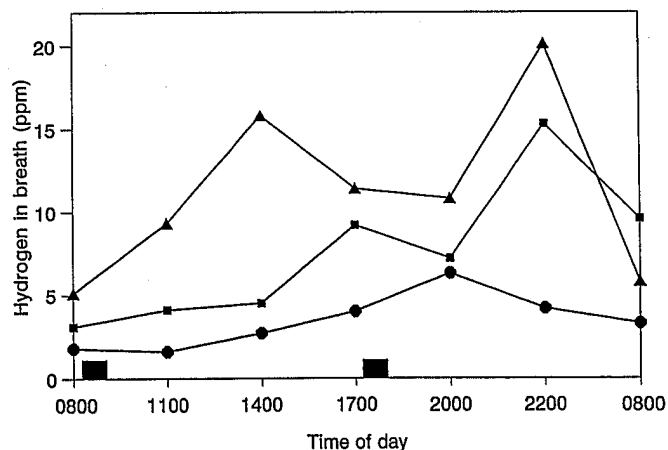


FIGURE 1. Mean breath-hydrogen concentration on the seventh day of supplementation with placebo (●), fructooligosaccharides (▲), or resistant starch (■). Bars on the horizontal axis indicate time of ingestion of supplement.

ground diet (12–14). In a previous study (29), we found no fructooligosaccharides in feces of healthy men after supplementation with 15 g fructooligosaccharides (30). Thus, colonic bacteria are evidently capable of fermenting 100% of fructooligosaccharide supplements in subjects with a complete colon. In our subjects with a pouch, the proportion was 83%.

Mean fecal excretion of residual starch during placebo consumption was 5 g; this can be attributed to resistant starch in the background diet. Average recovery of resistant starch from the supplement dose was 54%. In healthy subjects, ≈ 20 –30% of resistant-starch supplement was recovered from feces (31). Patients with a pouch thus had more efficient fermentation of fructooligosaccharides than of resistant starch, but both nondigestible carbohydrates were fermented less extensively in such patients than in subjects with an intact colon.

Bowel habits and stool composition

An ileal pouch has a much smaller mucosal surface available for water resorption and a smaller volume than an intact colon. Thus, luminal contents that pass the pouch are relatively large compared with those in an intact colon. The pouch fills up sooner, which results in a shorter stasis time of luminal contents and faster transit (1, 32). Low resorption of water from luminal contents causes a higher stool weight and a lower proportion of dry matter than in subjects with an intact colon. During placebo supplementation, the mean fecal wet weight was 541 g/d, with 12.5% dry matter. Supplementation with fructooligosaccharides significantly increased 24-h fecal weight and fecal dry mass, although $< 10\%$ of the increase in fecal mass consisted of unfermented fructooligosaccharides. The proportion of fecal wet material was not affected by fructooligosaccharides; therefore, the increased fecal weight was probably not caused by an osmotic effect of fructooligosaccharide molecules. It was more likely due to an increase in fecal biomass, which is also found in healthy subjects (33).

Administration of resistant starch did not significantly alter fecal wet or dry weights. Unfermented resistant starch would be expected to have its greatest effect on fecal dry weight. Because of the lower apparent fermentability of resistant starch, a smaller effect on biomass, reflected in fecal wet weight, might be expected. Intraindividual week-to-week variations in fiber intake possibly masked a small effect of resistant starch on dry weight and biomass.

The brief duration of stasis of luminal contents in the pouch was also reflected in the frequency of defecation. During the control period, patients reported a mean of 6.5 stools/d, which is similar to quantities found by other researchers (7, 8, 34). During fructooligosaccharide supplementation, the frequency was even higher, probably as a result of the higher stool volumes. The mean time between pouch voidings was < 4 h. This interval was obviously long enough to allow bacteria to degrade most of the fructooligosaccharide supplement. Because fermentation of resistant starch is relatively slow, the interval between voidings may have been too short for microflora to ferment the resistant starch more extensively.

Breath hydrogen and fecal short-chain fatty acids

Bacterial degradation of fructooligosaccharides and resistant starch was reflected in the production of hydrogen and short-chain fatty acids. Bruun et al (10) observed an increase in

breath hydrogen in half of patients with a pouch who took the synthetic nondigestible disaccharide lactulose (10 g). Only 2 of the 15 subjects in that study had a hydrogen response to wheat starch. Those who did not respond to lactulose had poor functional pouch characteristics, such as incontinence. Bruun et al concluded that fermentation of lactulose is associated with better pouch function.

In our study, fructooligosaccharide supplementation increased hydrogen excretion by 236% relative to placebo values and resistant starch increased hydrogen excretion by 147%. During supplementation with either fructooligosaccharides or resistant starch, half of the subjects did not respond, that is, their hydrogen concentrations in expired air were never > 10 ppm. We did not find any significant correlations between hydrogen excretion and recovery of fructooligosaccharides or resistant starch in feces. This may indicate that hydrogen response was determined by factors other than the mass of carbohydrates fermented. However, because of the small number of patients and the small range in fecal carbohydrate excretion, we may have missed a modest association.

Our data do not allow firm conclusions about the effect of either fructooligosaccharides or resistant starch on the total amount of short-chain fatty acids or on fecal pH. Short-chain fatty acids are produced simultaneously with hydrogen by most bacteria (35). MacFarlane et al (36), in an autopsy study of victims of sudden death, found high amounts of short-chain fatty acids in the proximal colon and lower amounts toward the end of the gastrointestinal tract. They attributed this to rapid absorption of these acids by the colonic mucosa. A similar absorption by pouch mucosa could explain why we did not find significant effects on total excretion of short-chain fatty acids or on pH in our study. We observed trends toward a greater excretion of total short-chain fatty acids, a greater excretion of acetate, and a lower fecal pH but our study probably lacked the power to detect small effects on these variables. Tonelli et al (37) found no increase in fecal short-chain fatty acids after administration of short chain-fatty acids into the pouch. They concluded that rapid absorption by pouch mucosa was probably responsible.

Fructooligosaccharide supplementation significantly depressed excretion of isobutyrate and isovalerate. These short-chain fatty acids originate from bacterial breakdown of amino acids (38–40). Similar effects were observed in healthy men given galactooligosaccharides (41) or lactulose (42, 43). Protein fermentation was thus apparently depressed by the addition of a rapidly fermentable carbohydrate. Protein fermentation produces not only amino acid-derived short-chain fatty acids but also indoles and ammonia. These products might have a toxic effect on mucosa (44–46). Therefore, we suggest that adding fructooligosaccharides to the diet of patients with an ileal pouch–anal anastomosis might decrease cytotoxicity of pouch contents.

Resistant starch increased excretion of butyrate, an effect also found in studies in healthy subjects (31, 47). Butyrate is a major fuel for the colonic mucosa and may inhibit cell proliferation and stimulate cell differentiation. Moreover, it was suggested that ulcerative colitis is caused by diminished oxidation of butyrate (48). Additionally, Nasmyth et al (4) observed a negative correlation between concentration of butyrate in pouch effluent and severity of villous atrophy of pouch mucosa. Thus, it may be worthwhile to study the potentially

beneficial effects of dietary resistant starch in patients with pouch inflammation.

Inflammation of the ileal pouch (pouchitis) is often regarded as a new manifestation of ulcerative colitis because pouchitis is far more common in patients who were operated on because of ulcerative colitis than in those operated on because of familial adenomatous polyposis (34, 49). In this study, we intended to study fermentation in a group of healthy patients with an ileal pouch-anal anastomosis. The patients had never had any clinical signs of pouchitis but we did not confirm the absence of pouchitis by endoscopic or histologic examinations of the pouch. Moreover, some of the patients were taking medications (loperamide and prednisone) that could have masked symptoms of pouchitis. As a result, we might have unintentionally included some patients with pouchitis in our study.

Bacterial overgrowth was previously considered a cause of pouchitis (4, 5, 50). There is, however, no theoretical foundation for such an effect. Additionally, bacterial overgrowth of the pouch is present in virtually all patients with a pouch, independent of the presence or absence of pouchitis. Microbial analyses of pouch effluents did not find higher bacterial counts in patients with pouchitis than in those without pouchitis (51–53). Thus, bacterial growth does not contribute to pouchitis. In fact, there are indications that pouch flora may help maintain pouch health. A relative increase in aerobic bacteria and decreased production of short-chain fatty acids—both possibly caused by a low supply of fermentable saccharides—were associated with pouchitis (8). Also, Bruun et al (10) found that the ability to ferment lactulose, measured as a breath-hydrogen response, was associated with better pouch function.

Conclusions

Ileal pouch flora was competent to ferment nondigestible dietary carbohydrates. Fructooligosaccharides were largely fermented and they depressed protein fermentation. Resistant starch caused an increase in excretion of butyrate. It appears justified to study the effects of such dietary carbohydrates on the development of pouchitis. ■

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