Fate of Soluble Carbohydrate in the Colon of Rats and Man

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ABSTRACT The fate of glucose in the colon of rats and man was investigated by measuring breath \(^{14}C\)CO\(_2\) and fecal \(^{14}C\) after direct instillation of \(^{14}C\)-labeled glucose, acetate, and lactate into the cecum. For the 6 h after administration of as much as 400 mg of [U-\(^{14}C\)]-glucose to the rat and 12.5 g to man, \(^{14}C\)CO\(_2\) excretion was as rapid after intracecal as after intragastric instillation. Less than 20\% of \(^{14}C\) instilled into the cecum as glucose was recovered in feces and only about 15\% of this fecal \(^{14}C\) was in a dialyzable form. The conversion of intraceally administered glucose to CO\(_2\) was dependent upon the presence of the colonic flora, as evidenced by the minimal excretion of \(^{14}C\)CO\(_2\) after administration of [\(^{14}C\)]glucose to germ-free rats. In contrast, acetate and lactate, fermentation products of glucose, were converted to CO\(_2\) as rapidly in germ-free rats as in their conventional counterparts. Measurement of \(O_2\) availability in the colonic lumen indicated that insufficient \(O_2\) was available for the aerobic metabolism of glucose by the colonic bacteria. These experiments suggest that the colon bacteria anaerobically metabolize most of the glucose to short-chain fatty acids, which are absorbed and oxidized by the host. Most of the remaining fecal glucose is converted to a larger molecular form that has limited osmotic activity. Thus, the colonic flora benefits the host by reducing the osmotic load of nonabsorbed carbohydrate and by making possible the salvage of a large percentage of the calories of carbohydrate, which is not absorbed in the small bowel.

INTRODUCTION

Carbohydrate malabsorption results in the deposition of osmotically active material in the large intestine. Since the osmolality of fecal water is only slightly greater than that of plasma (1), failure to absorb or metabolize this carbohydrate in the colon results in an osmotic diarrhea. The magnitude of such carbohydrate-induced diarrhea should be markedly influenced by the metabolism of the colonic bacteria. A major metabolic pathway of these bacteria is the anaerobic breakdown of carbohydrate to a variety of short-chain fatty acids, a reaction that might markedly increase the osmotic load. For example, glucose can be converted to several fatty acids by bacterial fermentation (2). At the pH of the colon, the fatty acids would be present in the ionized form and, if not absorbed or metabolized, these acids would hold an equal number of milliequivalents of cation in the lumen. Thus failure to absorb just 10 g or 55 mosmol of glucose in the small bowel could result in a 220 mosmol load in the colon, or the isotonic equivalent of about 650 ml of fecal water. However, if these fatty acids were absorbed from the colon or further catabolized in the colon to CO\(_2\) and H\(_2\)O, bacterial metabolism might actually reduce the osmotic load.

The purpose of the present study was to investigate the ultimate fate of unabsorbed carbohydrate in the colon of rats and man, with particular reference to bacterial metabolism. These studies demonstrate that bacterial fermentation makes possible the absorption of a large fraction of the carbohydrate deposited in the cecum, thus salvaging calories as well as minimizing fecal water.

METHODS

Animals and operative techniques. Male, Sprague-Dawley rats weighing about 250 g were employed in most studies. Germ-free rats used in certain experiments were obtained from Charles River Breeding Laboratories (Wilmington, Mass.).

To study quantitatively the metabolism of materials in the cecum, one end of a Silastic catheter (76 \(\mu m\) inside diameter) was implanted in the cecum. Via a subcutaneous tunnel, the catheter was brought out at the back of the neck, where it could not be reached by the rat. At least 3 wk were allowed for recovery from surgery before studies were initiated. The rats were not restrained and were allowed to eat a standard rat chow diet before and during the studies. In all experiments, the radioactive material was administered in 1 ml of 0.1 N PO\(_4\) buffer (pH 6.5), and the tube was then cleared with the injection of 0.2 ml of air.
A polyethylene catheter was inserted into the stomach for the intragastric administration of test substance.

In other experiments, a laparotomy was performed under ether anesthesia to permit the direct instillation of material into the cecum of germ-free rats that did not have chronically implanted cannulas. Surgery was performed with sterile precautions and the study was carried out in a sterilized closed system. In these studies, the test dose was injected into the cecum with a 27-gauge needle. No leak of fecal contents was observed after removal of the needle. The abdominal incision was rapidly closed and the animal was then placed in the experimental chamber and allowed to regain consciousness.

Measurement of \(^{14}\)CO\(_{2}\) excretion. The rat was placed in a polystyrene chamber (gas space approximately 800 ml) previously described (3). Room air was constantly aspirated through this chamber at a rate of about 250 ml/min and through 4 ml of a 1:1 mixture of 0.5% Hyamine hydroxide (Rohm & Haas Co., Philadelphia, Pa.) and methanol in a scintillation vial, and lastly through a sintered glass filter submerged in a 20-cm-deep column containing 200 ml of the Hyamine-methanol mixture. Phenolphthalein was added to the absorbing fluid to serve as an indicator of pH, and, hence, saturation of the Hyamine with CO\(_{2}\). Both the scintillation vial and the column were immersed in ice baths to minimize evaporation. Preliminary studies showed that about 85% of the CO\(_{2}\) was trapped in the scintillation vial, and negligible CO\(_{2}\) escaped from the fluid in the column. The radioactivity of the fluid in the scintillation vial, which trapped 2 mmol of CO\(_{2}\), was used for serial specific activity determinations, and the total \(^{14}\)CO excreted was calculated from the sum of the radioactivity in the vials and the fluid in the column. Radioactivity was determined by adding 15 ml of Fluorolloy (Beckman Instruments, Inc., Fullerton, Calif.) to 4 ml of trapping fluid and counting to \(\pm 2\%\) accuracy in a liquid scintillation counter.

Fecal recovery of \(^{14}\)CO\(_{2}\), and polyethylene glycol (PEG). Stools were collected for a 4-day period after administration of 100 mg of PEG and the radioactive test substance. To minimize coprophagia, the rats were supported on a very coarse screen in the experimental chamber used for \(^{14}\)CO\(_{2}\) measurements and then were housed for the next 4 days in metallic cages. The entire 4-day stool output was homogenized in about 100 ml of water. To determine the total \(^{14}\)C in feces, an aliquot was analyzed by combustion in a Packard Tri-Carb Oxidizer (Packard Instruments Co., Inc., Downers Grove, Ill.). The dialyzable radioactivity of the feces was determined by equilibrium dialysis. A 5-ml aliquot of the fecal homogenate was dialyzed for 72 h against 5 ml of water at 3°C. Aliquots of the dialysate obtained at 1, 2, and 3 days were analyzed for radioactivity. The PEG concentration of an aliquot of the homogenized 4-day stool collection was determined by a standard turbidimetric method (4). The fecal recoveries for \(^{14}\)C are expressed in both the uncorrected form, as well as corrected for incomplete recovery of PEG. Since the \(^{14}\)C-to-PEG ratio probably does not remain constant from one fecal specimen to the next, this correction may not be entirely accurate. However, it seems likely that the corrected value is closer to the true value than the uncorrected one and, therefore, the values corrected for PEG will be employed in the discussion of the results.

Carbon monoxide absorption from the colon. In an attempt to estimate how fast O\(_{2}\) was delivered to the colonic lumen, CO absorption was measured. Under ether anesthesia, the abdomen was opened and a catheter was inserted into the cecum via the distal ileum and secured with a ligature around the ileum. An occluding ligature was also placed around the rectosigmoid junction. The catheter was brought out through the abdominal incision, which was then closed. After the animal regained consciousness, 2.0 ml of CO was instilled through the catheter, which was then occluded. This volume of CO filled but did not overly distend the cecum. After 20 min had elapsed, the rat was sacrificed and the colon between the ligatures was rapidly dissected free. To determine how much CO remained in the colon, the gut segment was placed in a 100-ml syringe. The catheter inserted into the cecum was connected to a spinal needle inserted through a rubber diaphragm that sealed the tip of the syringe. The barrel of the syringe was then inserted. 20 ml of saline was rapidly injected into the gut via a second syringe, rupturing the gut segment and flushing out most of the CO. An additional 80 ml of air was flushed through the gut segment and the 100-ml syringe was then vigorously agitated. The amount of CO absorbed was determined by subtracting the residual CO from the amount initially instilled. To test the completeness of CO recovery by this technique, CO was instilled into the cecum of two rats, sacrificed immediately. The recovery in these two experiments were 97% and 101% of the amount instilled. CO concentration was determined by gas chromatography (Beckman GC-5) with a \(9"\times 4"\) stainless steel column packed with molecular sieve, an oven temperature of 115°C, argon as the carrier gas, and a thermal conductivity detector.

The rate of colonic blood flow that would have become saturated with CO (F\(_{\text{CO}}\)) was calculated from the formula:

\[
F_{\text{CO}} = \frac{Q_{\text{CO}}}{1.36 \times [\text{Hgb}]}
\]

where \(Q_{\text{CO}}\) is the observed absorption rate of CO and 1.36 is the volume of CO bound per gram of hemoglobin.

Human studies. Four healthy volunteers were intubated with a mercury-weighted polyvinyl tube, passed until the tip was fluoroscopically located in the cecum. Via the tube, a solution containing 12.5 g of glucose, 5 μCi of [U-\(^{14}\)C]-glucose, and 2 g of PEG in 300 ml of water was instilled into the cecum over a 20-min period. Breath \(^{14}\)CO\(_{2}\) specific activity was monitored by having the subject periodically exhale (at \(\frac{1}{4}, 1, 2, 3, 4, 6, 8, 10, 16, 24\) h) through 4 ml of the Hyamine-methanol solution described in the rat studies. Total \(^{14}\)CO\(_{2}\) excretion was estimated by assuming that total CO\(_{2}\) output for the subjects was about 9 mmol/kg body wt/h (5). All stools passed for 4 days after glucose instillation were analyzed for total \(^{14}\)CO, dialyzable \(^{14}\)C, and PEG, as described in the rat studies. Several weeks after the initial study, the subjects ingested the same quantity of PEG and [U-\(^{14}\)C]-glucose, and breath \(^{14}\)CO\(_{2}\) and stool \(^{14}\)C excretion were once again similarly monitored.

To estimate the rate at which O\(_{2}\) became available for intraluminal oxidation reactions, a constant gas perfusion technique (6) was used, as follows. The cecum of three healthy subjects who had fasted for 12 h were intubated with mercury-weighted polyvinyl tubes. To prevent swallowed nitrogen or oxygen from entering the colon from above, the stomach was constantly aspirated via a second tube for 4 h before the infusion as well as during the infusion. The colon was constantly perfused with argon at a rate of 45 ml/min and all gas passed per rectum was collected in 100-ml syringes via a rectal tube. The Na and O\(_{2}\)

**Fate of Carbohydrate in the Colon**
concentrations in each syringe were analyzed by gas chromato
graphy and the concentration of each gas in each
syringe was then plotted against the time of collection of
the sample in the form of washout curves, as has been
previously described (6). The concentrations of these gases
in the initial sample were relatively high but then fell off
rapidly, reaching a low, relatively constant concentration
that persisted indefinitely. The rate at which \( O_2 \) was washed
out during this steady state should represent the rate at
which \( O_2 \) diffuses into the colon in excess of the basal (fast-
ing) utilization in the colon, because the argon infusion
produces a maximal \( O_2 \) gradient between blood and lumen.
An estimate of the rate of \( O_2 \) delivery to the colonic mucosa
was calculated by measuring the blood flow required to
deliver the \( N_2 \) washed out during the steady state. By
assuming perfect equilibration between blood and lumen, the
rate (in milliliters per minute) is calculated from:
\[
Q = \frac{P_L - P_B}{V_s \cdot \gamma \cdot \Delta N_2}
\]
where \( V_s \) is the solubility of \( N_2 \) in
blood (12.8 ml/ml, \( \text{stn} \)), and \( P_B \) and \( P_L \) are the partial
pressures of \( N_2 \) in blood and lumen, respectively.
Rearranging the above yields: \( F_1 = \frac{Q}{aN_2 (P_B - P_L)} \).

RESULTS

Excretion of \(^{14}\)CO\(_2\) and fecal \(^{14}\)C recovery in rats. Ta-
ble I summarizes the results (mean±1 SEM) of mea-
surements of \(^{14}\)CO\(_2\) excretion and 4-day fecal recovery of
\(^{14}\)C after intracecal or intragastric administration of
\(^{14}\)C-labeled compounds to conventional and germ-free rats.

After intracecal administration of the [\(^{14}\)C]glucose
tracer quantities or with 100, 200, and 400 mg of un-
labeled glucose, \(^{14}\)CO\(_2\) excretion over the next 6 h aver-
gaged 57.8±1.4, 48±3.3, 42.7±3.9, and 42.8±2.4%,
respectively, of the instilled dose. This \(^{14}\)CO\(_2\) excretion
was actually slightly greater than that observed after similar
injections were administered into the stomach, although the
differences are statistically signi-
ificant (\( P < 0.05 \)) only for the tracer and 100-mg doses. Fig. 1 compares the specific activity of excreted
\(^{14}\)CO\(_2\) after intracecal or intragastric administration of
100 and 200 mg of [\(^{14}\)C]glucose. It is apparent that the shape of the \(^{14}\)CO\(_2\) excretion curves are similar,
while the specific activity of \(^{14}\)CO\(_2\) is slightly higher at
each time period after intracecal administration.

This rapid conversion of intracecally administered
glucose to \(^{14}\)CO\(_2\) but not from the reflux of glucose
back into ileum, since virtually identical conversion of the
200 and 400-mg doses of [\(^{14}\)C]glucose to \(^{14}\)CO\(_2\) was
observed in four rats when the terminal ileum was
ligated immediately before injection of the glucose load

<table>
<thead>
<tr>
<th>TABLE I</th>
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<tr>
<td><strong>(^{14})CO(_2) and Fecal (^{14})C Excretion after Intracecal and Intragastric Administration of (^{14})C-Labeled Glucose and Organic Acids to Conventional and Germ-Free Rats</strong></td>
</tr>
<tr>
<td>Animal</td>
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</tr>
<tr>
<td>Conventional rat</td>
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* Results reported as means±1 SEM.
into the cecum. The percentage of the dose appearing as 
\(^{14}\text{CO}_2\) in the first 6 h averaged 44% and 42% for the
200-mg and 400-mg doses, respectively.

Fecal recovery studies showed that less than 20% of
the \(^{14}\text{C}\) of the [U-\(^{14}\text{C}\)]glucose instilled into the cecum
was excreted in the stool (see Table I). Equilibrium
dialysis of six fecal samples indicated that an average of
only 15\(\pm\)3.6% of the radioactivity was dialyzable. When
0.1 \(\mu\)Ci of [\(^{14}\text{C}\)]acetate was added directly to three,
5-ml aliquots of fecal homogenes and then dialyzed as
described above, a mean of 101% was found to be in a
dialyzable form.

The rapid conversion of intracecally administered
\(^{14}\text{C}\) to \(^{14}\text{CO}_2\) was clearly dependent upon the presence
of the colonic bacteria. Fig. 2 shows the specific
activity of \(^{14}\text{CO}_2\) excreted by germ-free rats after instilla-
tion of 200-mg doses of [U-\(^{14}\text{C}\)]glucose, [1-\(^{14}\text{C}\)]acetate,
or [U-\(^{14}\text{C}\)]lactate into the ceca of germ-free rats. [U-
\(^{14}\text{C}\)]glucose was very slowly converted to \(^{14}\text{CO}_2\), while
the conversion of [1-\(^{14}\text{C}\)]acetate and [U-\(^{14}\text{C}\)]lactate to
\(^{14}\text{CO}_2\) was as rapid in the germ-free animal as in their
conventional counterparts. Over 6 h, the germ-free ani-
mal excreted a total of only 2.2% of the [U-\(^{14}\text{C}\)]glucose
as \(^{14}\text{CO}_2\), while 51.5\(\pm\)6.7 of the [1-\(^{14}\text{C}\)]acetate and 42.0\(\pm\)
2.4 of the [U-\(^{14}\text{C}\)]lactate were metabolized to \(^{14}\text{CO}_2\) (see
Table I).

**Carbon monoxide absorption.** CO was absorbed at a
mean rate of 28\(\pm\)3 \(\mu\)l/min from the rat colon. The mean
hemoglobin concentration of the rats' blood was 13.1
0.2 g/100 ml. The rate of colonic blood flow that
would become completely saturated with CO was about
0.15 ml/min.

**Human studies.** The calculated breath \(^{14}\text{CO}_2\) excre-
tion and the fecal excretion of \(^{14}\text{C}\) after intracecal or
oral administration of 12.5 g of [U-\(^{14}\text{C}\)]glucose are
shown in Table II. As with rats, there was no signifi-
cant difference between the quantity of \(^{14}\text{CO}_2\) excreted
over a 6-h period after cecal administration (21.4\(\pm\)
2.4\%) as compared with that after oral administration
(20.8\(\pm\)2.0\%). In a given individual, the plots of the
expired \(^{14}\text{CO}_2\) against time after [U-\(^{14}\text{C}\)]glucose admin-
istration were remarkably similar, independent of whether
the glucose was administered by mouth or intracecally.
Fig. 3 shows typical specific activity curves obtained for
two of the individuals studied. A mean of only 14.2\(\pm\)

![Figure 1](image1.png) Figure 1: Comparison of the specific activity of \(^{14}\text{CO}_2\) excreted by rats after intracecal or intragastric administration of 100 or 200 mg of [U-\(^{14}\text{C}\)]glucose. Specific activity has been normalized for dosage instilled.

![Figure 2](image2.png) Figure 2: Specific activity of \(^{14}\text{CO}_2\) of germ-free rats after intracecal administration of 200 mg of [U-\(^{14}\text{C}\)]glucose, [1-
\(^{14}\text{C}\)]acetate, or [U-\(^{14}\text{C}\)]lactate.

<table>
<thead>
<tr>
<th>Table II</th>
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**\(^{14}\text{CO}_2\) and Fecal \(^{14}\text{C}\) Excretion after Oral and Intracecal Administration of \(^{14}\text{C}\)-Labeled Glucose to Healthy Human Subjects**

<table>
<thead>
<tr>
<th>Subject</th>
<th>(^{14}\text{CO}_2) excretion</th>
<th>Oral</th>
<th>Cecal</th>
<th>Fecal (^{14}\text{C}) recovery</th>
<th>Oral</th>
<th>Cecal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% dose/6 h</td>
<td></td>
<td></td>
<td>Uncorrected</td>
<td>Corrected for PEG</td>
<td>Uncorrected</td>
</tr>
<tr>
<td>1</td>
<td>16.4</td>
<td>17.2</td>
<td>0.074</td>
<td>0.12</td>
<td>8.8</td>
<td>14</td>
</tr>
<tr>
<td>2</td>
<td>19.6</td>
<td>21.0</td>
<td>0.67</td>
<td>1.32</td>
<td>14.5</td>
<td>15.5</td>
</tr>
<tr>
<td>3</td>
<td>21.2</td>
<td>19.0</td>
<td>0.62</td>
<td>0.70</td>
<td>3.9</td>
<td>8.0</td>
</tr>
<tr>
<td>4</td>
<td>26.0</td>
<td>28.3</td>
<td>0.47</td>
<td>0.52</td>
<td>12.2</td>
<td>19.4</td>
</tr>
<tr>
<td>Mean(\pm)SEM</td>
<td>20.8(\pm)2.0</td>
<td>21.4(\pm)2.4</td>
<td>0.46(\pm)0.14</td>
<td>0.67(\pm)0.25</td>
<td>9.85(\pm)2.30</td>
<td>14.2(\pm)2.4</td>
</tr>
</tbody>
</table>

*Fate of Carbohydrate in the Colon* 1161
2.4% of the \(^{14}\)C instilled into the colon was recovered in the stools. Equilibrium dialysis of fecal specimens from three of these subjects showed that an average of 17% (range, 14–20) of the fecal \(^{14}\)C was in a dialyzable form.

When the colon was constantly perfused with argon, \(O_2\) was washed out of the rectum at a mean rate of 0.16 ml/min (range, 0.10–0.24). \(N_2\) diffused into the colon under steady-state conditions at 0.36 ml/min. (range, 0.30–0.44 ml/min). The rate of blood flow required to deliver \(N_2\) at this rate (assuming perfect equilibration between blood and lumen) would be 38 ml/min. The \(O_2\) content of 38 ml of blood would be about 7.6 ml.

**DISCUSSION**

The rumen bacteria are known to play an important role in the nutrition of the ruminant, in that the organisms ferment otherwise indigestible polysaccharides to short-chain fatty acids, which are then absorbed and metabolized by the host (7). The following line of evidence suggests that the colonic bacteria of man and rat act similarly, thus permitting assimilation of carbohydrate that escapes absorption in the small intestine.

After direct instillation into the rat cecum of as much as 400 mg of \([U^{-14}\)C]\(\)glucose, only about 18% of the \(^{14}\)C was recovered in the feces. This apparent disappearance of \(^{14}\)C from the colonic contents was corroborated by the finding of rapid excretion of \(^{14}\)CO\(_2\) after intracecal administration of labeled glucose. In fact, conversion to \(^{14}\)CO\(_2\) for the first 6 h was at least as rapid after intracecal as after intragastric administration of the sugar. The possibility that glucose refluxed from the cecum into the ileum and then was absorbed from the small bowel was excluded by the finding of a similarly rapid excretion of \(^{14}\)CO\(_2\) when the ileocecal junction was occluded by a ligature.

This conversion of glucose to \(^{14}\)CO\(_2\) in the rat colon was clearly dependent upon the presence of the colonic bacteria. In germ-free rats only about 2% of a 200-mg load of glucose was converted to \(^{14}\)CO\(_2\) over 6 h, as compared to 43% in conventional rats. This low \(^{14}\)CO\(_2\) output could not be attributed to a general inability of the large cecum of the germ-free rat to absorb otherwise diffusible substances, since colonic administration of \([1^{-14}\)C]\(\)acetate or \([U^{-14}\)C]\(\)lactate resulted in \(^{14}\)CO\(_2\) excretion comparable to that observed in conventional animals.

There are two possible mechanisms whereby the colonic bacteria might make possible the conversion of glucose to \(^{14}\)CO\(_2\). First, the bacteria could oxidatively metabolize glucose to \(^{14}\)CO\(_2\), which would then be absorbed and excreted by the lungs or excreted in flatus. Second, the bacteria might anaerobically metabolize the sugar to fatty acids, which would then be absorbed and metabolized by the host. In an attempt to distinguish between these two possibilities, we estimated the rate of \(O_2\) delivery to the rat colonic lumen for oxidative metabolism by measuring the absorption rate of \(CO\) from the large intestine. Hemoglobin binds equal quantities of \(O_2\) and \(CO\) and these two gases have roughly comparable diffusion coefficients. Thus, the rate of \(CO\) absorption will provide an estimate of the rate of \(O_2\) delivery to the lumen. This estimate should be maximal, since a higher partial pressure difference existed between blood and lumen for \(CO\) than for \(O_2\) and thus \(CO\) might diffuse more rapidly. In addition, a sizable fraction of the \(O_2\) delivered to the colonic mucosa would be utilized by the mucosa as well as by reactions other than glucose oxidation in the lumen. Thus, the actual available \(O_2\) would be only a small fraction of the 1.68 ml/h delivery rate observed for \(CO\).

Since the observed conversion to \(^{14}\)CO\(_2\) of 40% of the 400 mg of glucose in the cecum would have required about 120 ml of \(O_2\) over a 6-h period, it is apparent that insufficient \(O_2\) could have been available in the lumen to permit oxidative metabolism of the glucose by the colonic bacteria. Thus it seems necessary to postulate that bacteria anaerobically metabolized the glucose, with volatile fatty acids presumably being the major product. Depending upon the fermentation pathway, this reaction could release a variable quantity of \(CO\) up to a maximum of 2 mol/mol glucose. The remainder of the \(^{14}\)C removed from the fecal stream apparently resulted from the colonic absorption of the fatty acids with subsequent metabolism by the rat, per se. The ability of the colon to rapidly absorb fatty acids is demonstrated by the prompt conversion of intracellulally administered \([U^{-14}\)C]\(\)lactate and \([1^{-14}\)C]\(\)acetate to \(^{14}\)CO\(_2\) in the germ-free rat.

The possible role of cecal fermentation in the nutrition of the porcupine (8) and the rat (9) has been previously inferred from studies of the cecal fatty acids of the two species. These indirect studies suggested that
the cecal fermentation provided 16% of the total energy requirements of the porcupine (8) and 4.7% of that of the rat (9). In addition, recent studies have also demonstrated the conversion of carbohydrate to organic acids in the cecum of the pony (10) and the pig (11) and that these acids are transported across in vitro preparations of the colonic mucosa of these species.

The results of studies in four human subjects suggest that the fate of glucose in the colon of man is similar to that observed in the rat. Only 14.2±2.4% of a 12.5-g dose of [U-14C]glucose instilled directly into the cecum was recovered in the feces, despite correction for incomplete fecal collection with simultaneously instilled PEG. This apparent disappearance of [U-14C]glucose from the colon was confirmed by the finding of a breath 14CO2 excretion after intracecal instillation similar to that observed after oral ingestion of the sugar.

As with the rat, there appeared to be insufficient O2 available in the colon of man to allow for aerobic metabolism of the glucose. The observed conversion of 20% of the 12.5-g dose of glucose to CO2 over the first 6 h would require about 2 liters of O2. However, the perfusion of the large intestine with argon indicated that O2 accumulates in the colon of fasting subjects at a rate of only about 12 ml/h. To obtain a very rough estimate of the amount of O2 delivered to the colonic mucosa of the human subjects, mucosal blood flow was estimated by measuring the rate of Na+ accumulation in the colon and assuming perfect equilibration between blood and lumen for Na. The calculated mucosal flow for the entire colon was 38 ml/min, which would deliver about 7.6 ml of O2/min. Since these studies were carried out in fasting subjects, it is apparent that most of the O2 delivered to the colonic mucosa is consumed by the mucosa itself or by the "basal" metabolism of the colonic flora, leaving very little O2 available for the metabolism of malabsorbed carbohydrates.

The colonic bacteria appear to reduce the osmotic load of nonabsorbed carbohydrate by two mechanisms. First, the flora enables the colon to remove more than 85% of the nonabsorbed load from the lumen. In addition, equilibrium dialysis showed that an average of only about 17% of this fecal 14C was in a dialyzable form. Although studies were not carried out to determine the form of the nondialyzable 14C, it seems likely that this material represents structural carbon of the colonic bacteria. Thus, only about 3% of the glucose load instilled into the cecum in these studies appeared in feces in a form with appreciable osmotic activity.

This action of the colonic bacteria may be important in healthy subjects as well as in patients with gastrointestinal diseases. While there is no direct information on the amount of carbohydrate not absorbed after ingestion of a normal meal by healthy subjects, studies of H2 excretion provide indirect evidence that appreciable carbohydrate may routinely escape absorption in the small bowel. Virtually all H2 production in the gut occurs when fermentable substrate is delivered to the colonic bacteria (12). Appreciable H2 is excreted after ingestion of an ordinary meal by normal subjects, suggesting the failure to absorb dietary carbohydrate completely in the small bowel (13). The colonic absorption of bacterially produced organic acids may be the mechanism whereby the normal, formed stool is produced despite the failure of the small bowel to absorb material with an appreciable osmotic activity.

The limits of the ability of the flora to metabolize sugar were not tested in this study. The diarrhea usually observed after ingestion of 50 g of lactose by lactase-deficient subjects indicates that the metabolism to and/or absorption of short-chain fatty acids in the colon is insufficiently rapid to prevent diarrhea completely after such loads, although bacterial action might well reduce the volume of diarrhea.

The findings of this study stimulate a variety of questions on the role of the colonic bacteria in various diarrheal states. There are marked differences in the ability of lactase-deficient subjects to tolerate lactose. Is it possible that these differences result from different rates or pathways of lactose fermentation by the colonic flora? The diarrhea associated with lactose ingestion by lactase-deficient subjects often decreases after long-term feeding of lactose, despite the persistence of a flat lactose tolerance curve (14). Could this phenomenon be explained by the induction of a lactose-fermenting flora better able to metabolize the malabsorbed lactose? Could the frequently observed diarrhea associated with antibiotic ingestion result from failure of the altered flora to metabolize nonabsorbed material adequately? Lastly, since volatile fatty acids are the predominant anion of normal stool water (15), could functional diarrhea (or constipation) result from an inefficient (or excessively efficient) colonic flora?

Colonic bacterial metabolism also makes possible the conservation of calories in nonabsorbed foodstuffs that would otherwise be lost in the fecal stream. Since fermentation utilizes less than 10% of the available energy of glucose, absorption of the bacterial fermentation products allows for the recovery of most of the caloric value of malabsorbed sugars. While this mechanism is unlikely to be significant in health, it seems possible that the colon could become an important means of assimilating certain foodstuffs in patients with disease or resection of the small bowel.

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Fate of Carbohydrate in the Colon 1163
REFERENCES


