

*Leading article*

## Cellulose and the human gut

Cellulose consists of long unbranched chains of glucose, (1→4) β linked D-glucopyranose. In its pure form the straight chains are bound closely together by multiple intermolecular hydrogen bonds producing a water insoluble fibrous substance which is relatively inert. Modified celluloses such as ethyl and carboxymethyl derivatives, (widely used in the food industry), and methyl cellulose (which may be prescribed as a laxative or as an appetite suppressant), have very different chemical properties from pure cellulose. Their substituent groups disrupt the hydrogen bonding and the resulting compounds are more soluble. Much less is known of their fate and importance in the human gut. Cellulose is found in abundance in nature in virtually all plant tissues and is therefore a common component of our diet. Dietary cellulose is thought not to be digested in the stomach and small intestine, 85% being recoverable in ileostomy contents from subjects fed diets containing usually eaten foods.<sup>1 2</sup> In the large intestine however, it is fermented<sup>3-5</sup> by the microflora with the ultimate production of short chain fatty acids, hydrogen, carbon dioxide and methane.<sup>6 7</sup>

The metabolism of cellulose in man has long been a focus of interest, but progress has been hindered by a lack of accurate chemical methods for its measurement. Another reason is that native cellulose, as present in the plant cell wall, behaves differently in the gut from purified preparations which are extracted, usually by harsh treatments, from wood pulp. In this issue Kelleher *et al* (p 816) report their studies in which a single dose of <sup>14</sup>C-cellulose was given to each of 10 healthy subjects, who then collected faeces and breath samples for seven days in order to determine the extent of cellulose digestion and metabolism. Total recovery of <sup>14</sup>C was 73%, of which 57% was in faeces and 16% in breath. Wide variation was recorded between individuals, for example 47-80% of the dose was recovered in faeces. A surprising observation was the appearance in breath of <sup>14</sup>CO<sub>2</sub> within one hour of the test dose of <sup>14</sup>C-cellulose.

The labelled cellulose was prepared by exposing a growing plant to <sup>14</sup>CO<sub>2</sub> for 24 hours, then harvesting the leaves and isolating the polymer. Even after an extensive series of treatments to purify the cellulose the authors, to their credit, however, noticed that it still contained starch granules when they received it and they were able to remove a further 30% of the radioactivity by gelatinisation, starch hydrolysis and acid washing. The final radiochemical purity of the preparation is not reported, so that it remains possible that the test substance still contained small amounts of non-cellulosic material, which might account for the early appearance of <sup>14</sup>CO<sub>2</sub> in breath, as the authors suggest. In this case the actual digestibility of the cellulose would have been less than the observed 43%. On the other hand the exact chemical form of the <sup>14</sup>C excreted in faeces is unknown. Seven per cent was in the aqueous phase of stool, probably incorporated into a variety of low molecular weight substances, while in the solid phase

the  $^{14}\text{C}$  could be present in a number of forms such as microbial solids, undegraded cellulose, etc. In the absence of more precise information the degradability of this cellulose will probably be underestimated.

In the only comparable study of isotopically labelled cellulose degradation in the human gut, Carryer *et al*<sup>8</sup> used cellulose labelled with  $^{131}\text{I}$  iodine, prepared from filter paper as the iodobenzhydryl derivative. They recovered 87% of this material from the faeces of their subjects in five days. Again the chemical form of the isotope in faeces was not determined, leaving some doubt as to the extent of any degradation.

Ample evidence for breakdown of cellulose in man has been acquired by non-isotopic techniques and has been reviewed elsewhere.<sup>9</sup> Balance studies in humans where intake of dietary cellulose and faecal excretion have been measured and the source of cellulose was commonly eaten foods, such as fruit and vegetables and refined cereals, cellulose digestibility was of the order of 70–80%.<sup>3–5</sup> These and other reports have not unnaturally led to the study of cellulose metabolism in man in more detail, using purified forms of cellulose. Such preparations of cellulose have very different physical properties from the cellulose present in the plant cell wall and so lead to conflicting views of the role of cellulose in the gut. For example, in the work of Van Soest's group<sup>10 11</sup> in which healthy volunteers were fed controlled diets with the addition of cellulose from either cabbage, bran, or a purified cellulose (Solka Floc), average cellulose digestibility was 74% on the control diet, 75% in the cabbage, about 53% in the bran but only 25% from the Solka Floc. Moreover, the purified cellulose depressed the breakdown of other cell wall polysaccharides and reduced cellulose digestion in the subjects when they were changed to other diets. The capacity of colonic microorganisms to digest cellulose *in vitro* was also tested and in these studies the purified cellulose was virtually indigestible, while that from cabbage was extensively degraded. Similar findings were reported in 1936 by Williams and Olmsted<sup>12</sup> who fed three medical students cellulose from a wide range of food sources and observed that while 60–70% from carrot and cabbage was digested only 0–10% of a purified cellulose was broken down and 3–25% from cotton seed hulls.

In a different approach Betian *et al*<sup>13</sup> tried to isolate cellulolytic bacteria from the faeces of five human subjects using conventional microbial techniques. Only one subject apparently possessed such an organism. The test substance, however, was a purified cellulose obtained by making a slurry of Whatman no 1 filter paper. These findings contrast with those from balance studies of individuals, in which it is exceptional to find that cellulose from the plant cell wall is not degraded. Therefore the gut must almost universally contain cellulolytic bacteria. In studies on ruminants<sup>14</sup> purified celluloses are degraded much more slowly than those present in the cell wall and show a 10–15 hour lag before the onset of fermentation, a feature not seen in forage celluloses. Therefore, purified celluloses, while providing a more controlled approach to the study of cellulose metabolism, behave quite differently from native cell wall material. Perhaps experiments using purified, or modified material should not be directly extrapolated to what is going on during normal digestion.

Breakdown of cell wall cellulose is modified by several factors other than its chemical purity. In studies on ruminants the presence of lignin, cutin and silica all impair fermentation,<sup>15–17</sup> while in man the relative resistance

of cellulose, and other cell wall polysaccharides, of wheat bran to digestion<sup>5 10 12</sup> can be explained partly by its high lignin content relative to other human foods. Bran is about 3% lignin, while most fruit and vegetables contain only one-tenth of this amount.<sup>18</sup> The particle size of preparations containing cellulose also modify its rate of breakdown. When Heller *et al*<sup>19</sup> fed wheat bran to healthy volunteers at two different particle sizes, the cellulose in the coarse bran was only 6% digested, compared with 23% in the same bran finely ground. Surprisingly, the reverse happens in the ruminant, where fine particles leave the rumen earlier than coarse particles, being swept out more readily with the ruminant liquor and so spend less time in the gut and are less completely digested. Fine grinding of animal feeds therefore reduces their nutritional value.<sup>20</sup>

The time that cellulose spends in the gut fermentation chamber, whether that be the rumen, or the large intestine, is therefore important in determining the extent of its breakdown. This is certainly so in rumen studies<sup>14 21</sup> and evidence is also accumulating for this in man. In 1943 Hummel *et al*<sup>22</sup> noted that digestibility of cellulose was proportional to laxation rate (frequency of defaecation), less cellulose being digested in subjects who had more frequent bowel actions.

More recently Southgate and Durnin<sup>23</sup> observed that elderly men digested cellulose to a much greater extent than did young men and commented that transit of a marker dye through the gut was slower in the old. This hypothesis has been tested experimentally by Stephen,<sup>24</sup> who gave six healthy subjects a controlled diet containing ordinary foods and measured cellulose digestion and mean transit time. She then speeded up transit by giving the volunteers Senna and found that when transit time fell from 64 hours (control) to 35 hours (+ Senna), cellulose breakdown fell from 72% (control) to 48% (+ Senna). Kelleher *et al* in their paper in this issue chose to measure the metabolism of <sup>14</sup>C cellulose in two groups of volunteers, the elderly (average age 79 years), and the young (average age 44 years), in an attempt to explain the variation in digestibility between individuals. Cumulative recovery of <sup>14</sup>CO<sub>2</sub> in breath was significantly greater in the elderly (23% elderly vs 10% young) and faecal recovery was lower (52% elderly vs 64% young). This may indicate increased degradation in the elderly, provided that the assumptions made by the authors that CO<sub>2</sub> excretion of 9 mmol/kg body weight/h is equally true in both the age groups. Transit time measured as the recovery of 80% of an oral dose of radio-opaque pellets, was not significantly related to faecal cellulose recovery, although the data for transit are not given in the paper. In Stephen's studies<sup>24</sup> prolonging transit time from 47–88 hours with codeine phosphate did not significantly alter cellulose digestion (70% control vs 75% + codeine phosphate) and overall she has shown that when transit time is greater than about 50 hours the digestion of the cellulose fed in her study reached a plateau of about 75%.

Is there a physiological role for cellulose in the gut? In contrast with other cell-wall polysaccharides, purified cellulose, when given in reasonable quantities does not lower serum cholesterol concentration in man,<sup>25–27</sup> and only minimally increases faecal bile acid excretion.<sup>27 28</sup> Bile acids do not bind to cellulose *in vitro*.<sup>29</sup> By contrast, pure cellulose seems to impair absorption of minerals from the gut, when doses of between 10 and 21 g/day are given to healthy volunteers with controlled diets. Faecal

excretion of calcium, magnesium, iron, zinc and phosphate are increased and serum calcium, inorganic phosphate and iron concentrations fall.<sup>30-32</sup> Cellulose impairs glucose absorption in the rat,<sup>33 34</sup> but comparable studies have not been done in man.

The effects of cellulose on the large intestine have been studied in more detail. Doses of purified cellulose from 15–20 g/day given to volunteers in long term feeding studies lead to modest increases in stool output, shortening of transit time and a fall in stool pH.<sup>27 31 35-37</sup> In some animal studies cellulose may prevent colon cancer.<sup>38</sup> The mode of action of cellulose in the large intestine is probably related to its digestibility, because the water holding capacity of the material is very limited.<sup>39</sup> Breakdown of cellulose in the colon stimulates microbial growth, while any undigested cellulose provides a surface for bacteria, which may lead to the growth of specialised subpopulations.<sup>40</sup> Fermentation of cellulose, which requires a complex interaction of micro-organisms,<sup>41</sup> eventually produces short chain fatty acids: their importance has been reviewed elsewhere.<sup>42</sup>

Clearly cellulose can change gut function in man, and especially function of the large intestine. In practice, however, cellulose is present in our diet as part of the plant cell wall, where it is closely associated with many other carbohydrate polymers. In this form its effects are less predictable and more difficult to determine. Moreover the amount of cellulose in the United Kingdom diet is substantially smaller than that commonly used in experimental diets. Measuring the intake of cellulose in man is not easy, because of the difficulties of chemical analysis: published values for the cellulose content of commonly eaten foods vary 10-fold.<sup>18 43 44</sup> The best available analytical techniques, however, indicate that cellulose rarely contributes more than 20% of dietary plant cell wall polysaccharides.<sup>43</sup> Using these methods of analysis cellulose intake in the UK population is 4.7 g/day on average, while in four Scandinavian populations cellulose intake ranged from 3.2–4.2 g/day.<sup>45 46</sup> These quantities of cellulose are small and are unlikely to contribute to significant changes in gut function, or metabolism, independently of other cell wall polysaccharides. Whether native cellulose has unique properties in the human gastrointestinal tract remains to be established.

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