Introduction

Carbohydrates are responsible for 25–50% of daily energy intake. The carbohydrate composition of the diet changes with age. In breast milk and standard infant formulas, lactose is the only or predominant carbohydrate; starches and other sugars follow with the introduction of ‘beikost’. In the healthy, balanced diet of children and adults starches (and fiber) should prevail. The small bowel only absorbs monosaccharides, so dietary carbohydrates have to be hydrolyzed into their constituent monosaccharides glucose, galactose and fructose. Glucose and galactose are actively transported, while fructose absorption takes place through facilitated diffusion. Not all dietary carbohydrates can be hydrolyzed by human digestive enzymes. Unabsorbed carbohydrate enters the colon as a fuel for the gut microflora. While this is a physiologic process essential for normal colonic function, especially short-chain soluble carbohydrates may surpass the fermentative capacity of the colonic flora. Whether this leads to adverse reactions depends on several factors connected to both the carbohydrates involved and local variables. There is no absolute separation between normal and decreased carbohydrate absorption and malabsorption does not necessarily imply intolerance.

Here we present the present insights into carbohydrate malabsorption and intolerance, and discuss the clinical consequences, with emphasis on the consequences for the feeding of infants and young children. Whenever relevant, we refer to the Online Mendelian Inheritance in Man (OMIM) nomenclature and the 6-digit denominators used in this database.
Digestion and Absorption of Carbohydrates

Polysaccharides

Starches consist of variable combinations of amylose and amylopectin chains and, depending on their origin, have variable physicochemical properties. Amylose molecules are straight chains of glucose units with $\alpha$-1,4 bonds; amylopectin molecules have amylose backbones with additional $\alpha$-1,6-linked side chains. In native form, starches are more or less inaccessible to amylase. Heating (cooking), acidification and physical degradation loosen the knots of starch granules and render them more accessible for enzymatic cleavage. Amylose digestion is primarily cared for by $\alpha$-amylase. This acts only on interior $\alpha$-1,4 bonds, releasing maltose (2 glucose units) and maltooltriose (3 glucose units). Amylase only partly degrades amylopectin, leaving remnants of up to 6 glucose units with at least one $\alpha$-1,6 bond: $\alpha$-limit dextrins. Further degradation is provided by the brush border enzymes maltase-glucoamylase (short glucose polymers and starch $\alpha$-1,4 bonds) and sucrase-isomaltase (oligosaccharide $\alpha$-1,4 and $\alpha$-1,6 bonds). Starches need processing (milling, cooking) to be digestible and part of the starch content of any given meal will resist digestion and enter the colon. This may have greater impact on colon function in infants and small children than in adults [1].

Oligosaccharides and Disaccharides

All carbohydrates have to be split into monosaccharides before they can be absorbed by the gut epithelium. At the brush border level, three enzyme complexes are available: the $\alpha$-galactosidases, sucrase-isomaltase and maltase-glucoamylase; and the $\beta$-galactosidase, lactase (also called lactase-phlorizin hydrolase). Sucrase-isomaltase hydrolyzes sucrose as well as maltose, maltotriose and $\alpha$-limit dextrins, while lactose is exclusively degraded by lactase. Some dietary disaccharides and oligosaccharides are not digested by any of these enzymes. These include fructans from the Allium species, raffinose and stachyose from beans, as well as the laxative lactulose. Interestingly, breast milk contains high concentrations (3–15 g/l) of non-absorbable carbohydrates. Over 100 different oligosaccharides are identified and, apart from favorably affecting fecal consistence, their main role is to establish a healthy colonic microflora by the suppression of potential pathogens. Recently, infant formula has been marketed containing indigestible fructo- and galacto-oligosaccharides, which should mimic the ‘fiber’ function of human oligosaccharides.

Lactase (OMIM 603202) hydrolyzes lactose and many other $\beta$-glycosidic molecules. It is a 1927-amino acid protein which is present in the brush border as a dimer [2]. Different from the $\alpha$-glycosidases, its activity is low up to 30 weeks of gestation and peaks at term. Lactase activity remains high for the first 3–4 years of life and thereafter normally decreases: adults are left with 5–10% of newborn activity. This loss of lactase activity is caused by genetic
imprint: the lactase gene turns to low activity, and less lactase makes it to the brush border (‘adult-type hypolactasia’). In this respect, mankind does not renounce its origin: in all mammals, lactase activity declines after weaning. In contrast, most Caucasians keep high (but slowly declining) lactase activities throughout their lives [1, 3]. The ability to digest lactose as an adult (‘lactase persistence’) is thought to be caused by a mutation which may stem back from about 10,000 years ago, at the dawn of dairying. Recent research suggests that the present distribution of lactase persistence in Europe is a reflection of gene-culture co-evolution between milk-producing cattle and humans [4]. Especially Asian and African populations have high (80–100%) percentages of adult-type hypolactasia; in Western Europe, hypolactasia is more prevalent in the Mediterranean area (~40%) than in Scandinavia (~5–10%) [5].

**Monosaccharides**

The absorption of glucose, galactose and fructose across the brush border and subsequently across the basolateral membrane into the blood requires three transporters. The aldohexoses, glucose and galactose, are co-transported with Na\(^+\) from the intestinal lumen into the cytosol by SGLT1 (OMIM 182380), while GLUT5 (OMIM 601843) is responsible for the facilitated, Na\(^+\)-independent transport of the ketohexose fructose. Passive transport out of the enterocytes through the basolateral membrane is provided for by GLUT2 (OMIM 138160). Extensive discussion of the properties of these transporters can be found elsewhere [3, 6]. Fructose absorption is often incomplete and this is also the case with other monosaccharides (such as xylose) and polyols (such as xylitol and sorbitol) present in certain foods.

**Indigestible Carbohydrates**

‘Dietary fiber’ includes both carbohydrates and other plant-derived substances, such as lignin. For the purpose of this review, we concentrate on the nonstarch polysaccharide fibers, including soluble (cellulose and hemicellulose B) and insoluble (hemicellulose A, pectins, gums, and mucilages) fibers [7]. Their common feature is that they cannot be degraded by human enzymes, but they are partially or completely fermented by bacterial enzymes. Cellulose, for instance, consists of chains of glucose units coupled with \(\beta-1,6\) bonds, resistant to human glycolytic enzymes. Dietary fibers are joined in the colon by resistant starch, indigestible oligo- and polysaccharides, and the undigested and unabsorbed fraction of mono- and disaccharides.

**Fate of Unabsorbed Carbohydrates**

**Colonic Microflora**

The colon is inhabited by a bacterial mass that by far outnumbers the total cell count of the human body. Carbohydrates are their main fuel source.
Malabsorption of Carbohydrates

About 30% of the colonic content consists of bacteria; feces contain between $10^{11}$ and $10^{12}$ bacteria/g, mostly anaerobes. Bacterial glycosidases degrade the available carbohydrates, resulting in the production of various products, including monosaccharides that are metabolized anaerobically to pyruvate, and lactate, to end up as gases (mainly carbon dioxide, methane and hydrogen) and short-chain fatty acids (SCFAs: acetate (52%), propionate (20%), butyrate (20%), and some branched-chain fatty acids) [8]. Under normal circumstances, about 90% of all SCFAs are absorbed. The bulk of the gases produced enter the circulation; carbon dioxide adds to the acid-base equilibrium and hydrogen and methane are expelled through the lungs. In short-bowel syndrome, bacterial shifts may lead to overproduction of D-lactate, which may result in encephalopathy and metabolic acidosis [9]. Presently, it is unclear if probiotics could play a role in improving carbohydrate tolerance by improving fermentation.

Colonic Salvage

The colonic mucosa absorbs SCFAs, which drag along water and electrolytes; monosaccharides stay behind in the fecal stream. SCFAs are subsequently utilized by mucosal cells (butyrate), liver (propionate and acetate) and other tissues (acetate). About 70% of the energy contained in unabsorbed carbohydrate is recovered through SCFAs. Butyrate accounts for 80% of the energy consumption of the colon; acetate may contribute up to 10% of the total energy expended in adults [10] and possibly considerably more in preterm infants [11]. This combined effort of microflora and colonocytes to save water and energy, reducing energy loss and fecal mass, has been dubbed colonic salvage [12]. Principally, this process is also active with carbohydrate malabsorption. Short-chain, soluble carbohydrates, such as lactose, however, increase small-intestinal transit time and therefore will more easily surpass the fermenting capacity of the microflora, thwarting the colonic salvage mechanism. On the other hand, the microflora as a whole is capable of adapting its metabolism to the types of carbohydrate supplied, increasing the salvage capacity [13, 14]. Consequently, the regular consumption of lactose in lactose malabsorption does not result in diarrhea, but rather in an increase in fecal (bacterial) mass [15]. Colonic salvage requires an established fecal microflora and a healthy colon of sufficient length. It may be less efficient in young infants and in toddler diarrhea, and it is impaired in antibiotic-associated diarrhea.

Role of Fecal Solids

Despite significant variation in the composition of the ileal contents that enter the colon and independent of total stool output, the water fraction of the feces of healthy individuals is kept within the narrow range of 70–75% [16]. The looseness of the feces in diarrhea is a function of fecal solid composition, the ratio of fecal water to water-holding capacity of insoluble
solids being increased [16]. Consequently, fat will increase the looseness of the stools, while fiber improves consistency. This may explain why the secondary lactose malabsorption found in enteropathy-associated diarrhea does not simply resolve with lactose exclusion from the diet. This also is relevant to toddler diarrhea: a low-starch, low-fiber diet reduces fecal water-holding capacity.

Role of Gut Motility

Rapid small intestinal transit results in less efficient absorption, perhaps the best example being the monosaccharide malabsorption that accompanies dumping syndrome [17]. In hypolactasia, the lactose digestion index (fraction of lactose absorbed) correlates with the orocecal transit time, but not with clinical symptoms [18]. A similar correlation exists in fructose absorption [19]. Conversely, carbohydrate malabsorption influences transit time in two ways. On the one hand, soluble carbohydrates that escape absorption will increase the osmolarity of the gut contents and thus speed up transit. On the other hand, SCFAs decrease gastric emptying through a hormonal pathway (the ‘colonic break’), which may improve carbohydrate absorption [20].

Malabsorption versus Intolerance

‘Carbohydrate malabsorption’ and ‘carbohydrate intolerance’ should not be used interchangeably. Malabsorption only indicates the amount or the fraction that escapes absorption, intolerance points at the clinical symptoms that may result. (Although the EAACI recently introduced a new nomenclature for adverse reactions to foods, in which there is no place anymore for the term ‘intolerance’ [21], we prefer the established term ‘lactose intolerance’ to the proposed ‘non-allergic hypersensitivity to lactose’.) When the supply of unabsorbed carbohydrates exceeds the fermentative capacity of the microflora, fermentation is incomplete, and not SCFAs but lactate and monosaccharides will prevail in the colon. This is a staged process and the end result depends not only on colonic salvage, bacterial adaptation and the type of solids present, but also on the type, the properties, the load and the rate of delivery of the carbohydrates involved. Mono-, di-, and oligosaccharides are rapidly but incompletely fermented, resulting in rapid accumulation of lactate and other small molecules and of gases. The osmotic load of these carbohydrates as well as the fermentation products is far greater than that of unabsorbed starches or fibers [22]. While fibers mainly increase fecal mass, oligosaccharides tend to increase gas production and water retention, and lactate and other breakdown products may irritate the bowel wall. This results in true carbohydrate intolerance, either as a combination of abdominal pain, distended abdomen, borborygmi and flatulence or as osmotic diarrhea, depending on the contributions of the individual factors. Figure 1 summarizes the events that accompany carbohydrate tolerance and intolerance.
Diagnosis of Carbohydrate Malabsorption

Several techniques have been developed to study carbohydrate malabsorption in clinical practice, including assessment of small bowel disaccharidase activities and tests in which various effects of the administration of carbohydrate loads are monitored, including the breath hydrogen test and the $^{13}$CO$_2$ breath test. For research purposes, the lactose digestion index can be estimated accurately with a test combining $^{13}$C-lactose and $^2$H-glucose [23]. For clinical use, however, we would advocate simpler means of assessing malabsorption. In infants, because of the short colonic transit time,
determination of fecal-reducing substances and pH gives the most reliable insight into the presence of carbohydrate malabsorption. In older children evaluated for hypolactasia or sucrase malabsorption, breath hydrogen tests are simple to perform and sufficiently reliable. In contrast, the breath hydrogen test is not sufficiently discriminatory for use in the evaluation of secondary lactose absorption in suspected enteropathy, as the test outcome depends on too many variables [24], or in fructose absorption, as it is also positive in healthy children [25]. In any case, clinical symptoms following the sugar load should be evaluated as well, for breath hydrogen increase denotes malabsorption and not intolerance and thus may be irrelevant to the clinical condition of the child. Often, therefore, clinical evaluation using a test period with a lactose-reduced diet is adequate for the diagnosis of lactose intolerance in hypolactasia. When awareness of the presence or absence of lactose in the diet could produce bias, lactose provocation might be evaluated in a double-blind fashion.

**Malabsorption of Glucose and Galactose**

Glucose and galactose are absorbed very efficiently and clinically relevant malabsorption of these monosaccharides is uncommon. Even in acute viral gastroenteritis, SGLT1-mediated glucose transport is sufficiently preserved to enable successful oral rehydration with glucose-electrolyte mixtures. In young infants, pancreatic α-amylase and maltase-glucoamylase (OMIM 154360) activities are too low to allow the use of starches in infant formula, although generally straight-chain glucose polymers are tolerated well. Low glucoamylase activity, both as a primary and a secondary condition, was found in 15 of 511 children with chronic diarrhea [26] and in 12 of 44 children with dyspepsia [27]. The implications of these findings have yet to be established.

**Glucose-Galactose Malabsorption (OMIM 606824)**

This condition is caused by mutations in the sodium-glucose transporter SGLT1 and presents itself with severe diarrhea from the first week of life, resulting in dehydration and growth failure. It may be fatal if glucose and galactose are not removed from the diet. Intolerance to these sugars persists throughout life. Fructose absorption is normal. About 300 cases have been identified [28].

**Secondary Monosaccharide Malabsorption**

Glucose malabsorption secondary to acquired enteropathy is rare since modern insights enable adequate parenteral and enteral nutritional rehabilitation in all patients regardless of the underlying disorder. It may accompany what was called ‘intractable diarrhea of infancy’, a vicious circle of malabsorption and malnutrition, in most cases probably initiated by infection.
Malabsorption of Carbohydrates

or food-sensitive enteropathy. ‘Intractable’ diarrhea with monosaccharide malabsorption is nowadays mainly found in short bowel syndrome, disorders of enterocyte architecture, such as congenital microvillus atrophy and intestinal epithelial dysplasia, and immune disorders including autoimmune enteropathy [29].

Malabsorption of Fructose

Since the first demonstration of incomplete fructose absorption in children [25], this phenomenon has gained much attention. It has become clear that GLUT5 has limited capacity for fructose transport [6]. Glucose improves fructose absorption (explaining why sucrose malabsorption is rare), which has been shown to be the effect of solvent drag, as amino acids have the same ability [30]. There is much debate on the possible health consequences of fructose malabsorption, including increased energy losses in young children [31] and metabolic disturbances [32]; from a practical point of view, these seem to be limited to aggravation of toddlers’ diarrhea, in which dietary imbalance is the central problem [33]. This extremely common phenomenon of incomplete absorption of fructose should be distinguished from a very rare condition, isolated fructose malabsorption, which is neither well defined nor caused by a mutation in GLUT5 [34].

Malabsorption of Sucrose

Disaccharide intolerance I (sucrase-isomaltase deficiency; OMIM 222900) results from mutations in the sucrase-isomaltase gene that result in five separate phenotypes [2]. Osmotic diarrhea starts the moment sucrose is introduced in the diet. On occasion even the presence of glucose polymers in infant feeding may cause diarrhea. Treatment consists of life-long exclusion of sucrose from the diet, if necessary combined with starch reduction. Recently, promising results have been booked with addition to the diet of sacrosidase, a liquid sucrase derived from the yeast *Saccharomyces cerevisiae* [35]. Secondary sucrose malabsorption, although less common than secondary lactose malabsorption, may be found in similar situations, especially in serious enteropathy and short bowel syndrome.

Malabsorption of Lactose in Infants

Lactose is the main carbohydrate source in the milk of virtually all mammals, and milk is the only dietary source of lactose. Human milk and humanized infant formula contain about 7 g/l of lactose; cow’s milk about 5 g/l.
The average 3-month-old infant therefore consumes some 10 g lactose/kg/day; the dairy consumption recommendations for young children would imply the consumption of 15–20 g lactose/day. Healthy infants have enough lactase to ensure adequate digestion of the lactose present in breast milk or formula. Lactase activity is, however, dependent on the integrity of the small bowel mucosa and enteropathy is invariably associated with low lactase levels. In The Netherlands, until a few years ago, a lactose-reduced formula was available for infants with ‘sensitive bowels’. The premise was that following acute gastroenteritis, the infant gut needed several weeks to recover and regain normal lactase levels. Nowadays, post-gastroenteritis enteropathy is considered the result of prolonged starvation due to too cautious refeeding; breastfeeding or standard formula should be continued during acute gastroenteritis.

**Term and Preterm Infants**

At birth, term neonates have higher lactase activities than at any moment before and after. They are optimally capable of digesting lactose. Preterm infants have low lactase levels, and seem to be not fully equipped for the consumption of human milk. Lactase activity increases rapidly after birth, however, and infants of less than 32 weeks gestation still digest at least 90% of the lactose consumed, while the lactose reaching the colon is efficiently salvaged and contributes to the energy accretion of the child [36]. Lactose intolerance is rare in this group and preterm infants should receive their mother's milk or humanized preterm milk as soon as they can tolerate enteral feeding.

**Congenital Lactase Deficiency (OMIM 223000)**

This is a very rare disorder, the vast majority of patients being identified in Finland. The symptoms are indistinguishable from those of glucose-galactose malabsorption [5]. Very recently a case of combined deficiency of lactase, maltase-glucosamylase and sucrase in an infant was published, possibly due to malfunction of some common regulatory factor [37]. Congenital lactase deficiency should be distinguished from congenital lactose intolerance (OMIM 150220), an even more unusual disorder (last reported in 1980) with vomiting, failure to thrive, dehydration, lactosuria, renal tubular acidosis, aminoaciduria, liver damage and cataract [38]. It is thought to result from increased gastric absorption of lactose. Although the disorder may be fatal if unrecognized, a lactose-free diet results in rapid recovery and after 6 months of age lactose is well tolerated.

**Secondary Lactose Malabsorption**

Secondary lactose malabsorption due to impaired lactase activity has been linked to poor growth in underprivileged children, possibly due to prolonged gastroenteritis-associated villus atrophy. It has also been suggested in several
studies (and refuted in others) that infantile colic is associated with transient lactose intolerance [39]. The etiology underlying this phenomenon is unclear. There is more proof for cow’s milk protein intolerance as a cause of colic [40], but the results of these studies may have been biased by the fact that cow’s milk protein-free formula is reduced in lactose as well (although oral therapy with lactase is not effective) [40]. Conversely, there seems to be no reason to exclude lactose from the feeding of cow’s milk-allergic children, even though lactose might theoretically be contaminated with cow’s milk proteins [41]. Lactose-reduced or lactose-free oligomeric or monomeric formula may be sporadically indicated in infants with ‘intractable’ diarrhea due to food protein-induced enterocolitis syndrome.

Malabsorption of Lactose in Older Children and Adults

*Adult-Type Hypolactasia (OMIM 223100)*

Although hypolactasia is actually the normal situation, it has certain disadvantages. The mutation resulting in lactase persistence enabled man to utilize cattle milk as an extra source of energy, increasing the chance of survival in times of famine. At present, cow’s milk has become a regular constituent of the Western diet; it is considered pivotal in the supply of calcium and vitamin B2 and therefore plays an essential role in the prevention of osteoporosis. Numerous studies have focused on the health consequences of hypolactasia. Not only the lactose digestion index, but also lactose tolerance is shown to vary considerably in between malabsorbers and also between adults and children. Small amounts of lactose are invariably tolerated by all adult malabsorbers [39], many of them tolerating normal amounts, while children in general seem to be more tolerant than adults [41]. Although lactase activity may start declining significantly in 3- to 4-year-olds, adverse effects will not reveal themselves for several years.

*Clinical Consequences of Hypolactasia*

The transition from lactose tolerance to intolerance is determined by several factors. The amount of ingested lactose that reaches the colon is influenced by the type of lactose-containing food; whether or not it is consumed with a meal; the remaining lactase activity; inter-current small bowel disease, and small bowel transit time. The efficacy of colonic salvage determines whether lactose is completely fermented or partly escapes fermentation. Only in the latter case, can symptoms of lactose intolerance ensue.

All too often, the diagnosis of hypolactasia is followed by the recommendation of considerably lactose-reduced or even lactose-free diets. Most individuals will tolerate considerable amounts of lactose. In adults, a single 6-gram dose of lactose is not followed by symptoms. Also, a microflora that is
exposed to a steady supply of lactose will adapt and increase its lactose-fermenting capacity, increasing tolerance [42]. Because of its health implications, lactose restriction should be applied with reticence, especially in children. Several simple measures may reduce the chance of symptoms after dairy consumption, including preferably using full-fat milk, in smaller portions and combined with a meal, partly replacing it by yogurt, and pre-incubating lactose-containing beverages with microbial β-galactosidases [42, 43].

Secondary Lactose Malabsorption

Although also in older children, the vulnerability of the brush border and especially lactase causes a rapid decline in lactase activity when the small bowel wall is damaged due to gastroenteritis, the extent of the damage is seldom large enough to give rise to clinically relevant lactose malabsorption. Dietary lactose restriction, therefore, is not indicated in toddlers and older children with acute diarrhea. To a lesser extent, the same holds true for enteropathy. Dietary restrictions, therefore, have to be dictated first and foremost by the underlying cause (e.g., food allergy or celiac disease) and lactose reduction is seldom indicated.

Conclusions

There is a tendency to overrate the impact of carbohydrate malabsorption on physical health. The main issue is that malabsorption does not necessarily imply intolerance. Colonic salvage enables the body to retain most of the energy contained in unabsorbed carbohydrates and prevents diarrhea. Only a few conditions, mostly presenting early in life, require targeted dietary measures. Secondary lactose malabsorption is generally a transitory problem and seldom necessitates dietary lactose reduction. Adult-type hypolactasia is not a problem until school age and can often be managed by simple measures. Further research should focus on the mechanisms regulating colonic salvage and the possible role of probiotics and prebiotics in this field [44].

References

Malabsorption of Carbohydrates


Malabsorption of Carbohydrates


Discussion

Dr. Gracey: I was interested that you didn't actually mention sucrase isomaltase deficiency by a name; I suppose you meant that it was covered by the rare syndromes in your last slide. The comment I would like to make is that, in ethnic groups with high rates of hypolactasia and very high rates of malnutrition and gastrointestinal disease, clinical lactose intolerance is a very significant problem.

Dr. Kneepkens: I fully agree as far as sucrase-isomaltase deficiency is concerned. As I was asked to concentrate on lactose and fructose, however, I left that out. As far as lactose malabsorption in underprivileged groups is concerned, there are a few studies addressing this problem in detail. On the one hand, there is a study from The Gambia showing that breastfed infants have more lactose absorption problems due to infections and undernourishment [1]. On the other hand, there is a study in older Tswana children from South Africa showing that all children with lactose malabsorption by nature can still tolerate lactose quite well [2]. They have more fecal production, but no symptoms other than that. So I guess it depends on age and on health whether or not lactose malabsorption is a problem.

Dr. H. Hoekstra: What would the problem of lactose intolerance in your population be: is it the lactase, is it the enteropathy, or is it a failure of normal physiological processes at the level of the colon?

Dr. Gracey: It is probably a combination of all. I am thinking particularly of a lot of studies done in Australia on aboriginal infants and children who have very high rates of malnutrition, who have environmental or tropical enteropathy and very high rates
of gastrointestinal infections and parasitic infestations. So you cannot simply disentangle one from the other. But this is a common problem in many parts of the tropics.

**Dr. Kleinman:** A number of gene polymorphisms are now associated with persistent lactasia and others with hypolactasia. Do you see any role for polymerase chain reaction, for example, in establishing lactose intolerance rather than using the breath test in children who are otherwise healthy?

**Dr. Kneepkens:** I really don’t know. One slide I didn’t show you presented the number of breath tests performed in our hospital, with a peak in the late 1980s of about 200/year, and it is now down to some 10/year. So we don’t use the breath test anymore in clinical practice because we don’t think we learn a lot from it. Most of the time the problem can be defined by just having a good history and physical; give advice to the children and wait how it turns out.

**Dr. Schmitz:** I was very much interested by the beginning of your talk regarding the bacterial metabolism in the colon and when you said that at the beginning the infant is more a lactate producer than an older child, which means that there is some kind of metabolic adaptation during development. Do you think, then, that the beikost or the solid foods, which are introduced during the normal feeding process between 6 and 18 months for example, always meet a competent microflora so that these additional foods are always very well metabolized or fermented, or do you think that sometimes there is incompetence of this colonic flora which makes the diversification of food problematic?

**Dr. Kneepkens:** Probably the flora has to learn to ferment the carbohydrates that are offered. That may be the reason why we have to be careful with the introduction of new foods to the children, giving the flora time to adapt. It is a matter of selection of the strains that are already present. While one strain is capable of fermenting a certain carbohydrate, another is not; so when you give this fermenting strain the time it will grow and do its work.

**Dr. Schmitz:** The question is whether it is one strain or a metabolic adaptation of a given strain. I don’t think there are much data on this point.

**Dr. H. Hoekstra:** It could be that motility is another important factor for the establishment of a certain flora and, even more interesting, whether a specific microbiota can influence motility.

**Dr. Benninga:** I have a question regarding motility. You showed that carbohydrates can cause diarrhea; but last year a paper came out suggesting that carbohydrate intolerance and constipation do play a role [3]. Could you speculate on how this works and if it exists?

**Dr. Kneepkens:** It is very difficult to envisage but the most important thing to realize in this respect is that carbohydrate malabsorption does not imply diarrhea. Of course it may lead to diarrhea, but it may as well lead to better fermentation and that may be the explanation, I couldn’t tell.

**Dr. Benninga:** In your practice have you seen many patients with cow’s milk allergy and constipation?

**Dr. Kneepkens:** Not one. But to come back to your previous question. At the time we were doing a lot of lactose breath tests, I remember that, while testing a child for abdominal pain, we found both constipation and lactose malabsorption. In those cases it is always difficult to choose between the therapies: on the one hand you would suggest decreasing lactose consumption, and on the other hand lactulose was the treatment for constipation, but it just doesn’t seem logical to do both at the same time. Perhaps a reduction in lactose intake would have been enough.

**Dr. H. Hoekstra:** May I add one comment on how to improve fermentation and the production of short-chain fatty acids in order to treat diarrhea. There was a study on cholera patients by Ramakrishna et al. [4] showing some effect with amylase-resistant
starch. With the European Working Group on Intestinal Infections we tried to repeat this kind of study using a prebiotic mixture of non-digestible carbohydrates with oral rehydration solution in non-cholera diarrhea, but it was ineffective [5].

References
