Gut Microbiota in Infants between 6 and 24 Months of Age

Seppo Salminen and Miguel Gueimonde

Functional Foods Forum, Program on Health Biosciences, University of Turku, Turku, Finland

Introduction

The indigenous microbiota of an infant’s gastrointestinal tract is created through complicated contact and interaction with the microbiota of the parents and the infant’s immediate environment. Nature-induced initial colonization is enhanced by galacto-oligosaccharides in breast milk and the microbiota of the mother. This process directs the later microbiota succession and health of the infant throughout the rest of his/her life [1, 2]. Thus, understanding and positive guidance of the process through dietary means is an important target when facilitating the mother–infant relationship through birth, breastfeeding, weaning and the first years of life. This process forms the platform for healthy gut microbiota throughout the entire life and is described in figure 1 [3, 4].

Stepwise Establishment of Microbiota

Source of Original Microbiota

The basis of healthy gut microbiota is created by the mother during pregnancy and microbiota transfer at birth. The microbiota of a newborn develops rapidly after birth and it is initially strongly dependent on the mother’s microbiota, mode of delivery and birth environment [1, 2]. The microbiota of the mother is determined by genetic and environmental factors. Recently, it has been suggested that stress and dietary habits during late pregnancy, prior to birth and at birth may have a significant impact on the microbiota at the time of delivery thus influencing the quality and quantity of first colonizers of the newborn. Subsequently, feeding practices including...
formula feeding and breastfeeding and the home environment of the infant influence the microbiota, both at the level of species composition and numbers of bacteria [1].

**Succession of Microbial Communities**

The stepwise process of establishing indigenous microbiota begins with facultative anaerobes such as the enterobacteria, coliforms, lactobacilli and streptococci first colonizing the intestine. These are rapidly succeeded by bifidobacteria and lactic acid bacteria [2, 4].

The establishment of the gut microbiota is usually characterized by the following steps: early colonization at birth with facultative anaerobes depending on the mode of delivery with rapid succession by anaerobic genera such as *Bifidobacterium, Bacteroides, Clostridium* and *Eubacterium* [4]. New molecular methods indicate that lactic acid-producing bacteria may account for less than 1% of the total microbiota while bifidobacteria can range from 60 up to 90% of the total fecal microbiota in breastfed infants. In formula-fed infants the microbiota is more complex, but depends on the composition of formula. New techniques indicate that the greatest difference in the microbiota of breastfed and formula-fed infant lies both in the bifidobacterial numbers and species composition within the intestinal microbiota, while the lactic acid bacteria composition appears to be rather similar. *Bifidobacterium breve, Bifidobacterium infantis* and *Bifidobacterium longum* are frequently found in fecal samples of breastfed infants, whereas the most common lactobacilli in both breastfed and formula-fed infant feces constitute *Lactobacillus acidophilus* group microorganisms such as *L. acidophilus, L. gasseri* and *L. johnsonii* [5]. In general, the differences between the

---

**Fig. 1.** Schematic description of the succession of gut microbiota during early life.
breastfed and formula-fed infants have decreased along with the development of improved composition infant formulas.

Characterization of the composition and function of the intestinal microbiota has been faced with considerable methodological difficulties and thus our understanding has improved stage by stage [3, 4]. As the disturbed succession during early infancy has been linked to the risk of developing infectious, inflammatory and allergic diseases later in life, it is still of great interest to further characterize both the composition and succession of microbiota during infancy [4–6].

**Weaning and Gut Microbiota: The Second Stage**

The practice of breastfeeding for 4–6 months has been considered to assist in the development of healthy gut microbiota. Major changes in the composition that occur during breastfeeding are related to breast milk components, especially galacto-oligosaccharides. Breastfeeding also provides an optimal environment for exchange of microbes between the mother and infant, including the contact with the mother’s skin and exposure to microbiota present in the immediate environment. As a result, every individual has unique characteristic microbiota during later phases of breastfeeding [1, 2]. Thus the intestinal microbiota as a defined entity does not exist, but this population comprises a dynamic mixture of microbes typical to each individual. At the moment, there are conflicting data on the microbiota of breast milk and this form of exposure needs to be reassessed [7].

Weaning and the introduction of solid foods as well as antimicrobial drug treatment periods will break the contact and constant supply of oligosaccharides and microbes from the mother. When characterizing the establishment of bacterial communities in 2 healthy babies for the first 10 months of life by several molecular methods, the following was reported. After delivery, the sterile gastrointestinal tract of an infant was rapidly colonized. During the first few days of life the colonization profiles were simple, but they became more complex as the bacterial diversity increased with time. Clone libraries of amplified 16S rDNA fragments allowed identification of the bacterial types by comparative DNA sequence analysis; the bacteria identified included members of the genera *Bifidobacterium*, *Ruminococcus*, *Enterococcus*, *Clostridium*, and *Enterobacter*. The species most closely related to the genera *Bifidobacterium* and *Ruminococcus* in particular dominated the intestinal microbiota based on stability over time and the numbers [8]. Deviations in intestinal microbiota during early life may predispose the infant to diseases later [9–12].

Thus, the basic target remains in a complex microbial community that provides the barrier against foreign microbes [1, 2, 4]. Additionally, this process creates the basis for the establishment of a ‘non-inflammatory’ status.
of the gut [4]. Such an environment in infants is distinguished by a large gram-positive bacterial population with a significant number of bifidobacteria in a species composition typical to the healthy infant (mainly *B. longum*, *B. breve* and *B. infantis*). Lactic acid bacteria may play a role in providing the right conditions for bifidobacteria to dominate. The collective composition of the colonizing strains in infancy also provides the basis for healthy gut microbiota later in life as the development of the disease-free state of the gut lies in the host–microbe interaction in infancy.

**Gut Microbiota in Infants from 6 to 24 Months**

*Microbiota*

Following the first 6 months of life the microbiota succession diverts towards a more diverse community [2, 8]. After weaning the differences observed between breastfed and formula-fed infants disappear due to the increase in the numbers of enterococci, *Bacteroides*, *Clostridium* and anaerobic cocci in the former group [6]. Increases in *Escherichia coli*, and enterococci have been reported after weaning. The levels of bacteroides and anaerobic gram-positive cocci [13] also appear to increase gradually during and following weaning, whereas enterobacteria decreased [8]. A recent pilot study by Rinne et al. [14] on 6-month-old infants and their fecal microbiota indicates that breastfed infants have high bifidobacterium levels and lower clostridial numbers than infants receiving either formula or formula with prebiotics. Adding probiotics to breast milk appears to reduce bacteroides and raise clostridia.

A small study reports the microbiota follow-up of 2 infants for a period of 2 years using molecular methods. At 6 months the T-RFLP profiles were dominated by *Bacteroides* and *Clostridium*. Between 6 and 12 months more species appeared in the feces of the infants, this increase in bacterial diversity has been reported by different studies. At 1 year there was a new shift in the microbiota and it became more diverse with *Bacteroides*, *Vellionella* and *Fusobacterium prausnitzii* increasing. The microbiota begins to resemble that of adults and there is a decrease in facultative anaerobes although these microorganisms still remain at higher levels than in adults [8]. Latter there may be a decrease in the levels of clostridia with a concomitant increase in a more diverse anaerobic microbiota including microorganisms such as fusobacteria and eubacteria [15]. Contrary to that, other studies [16] reported that in 10- to 18-month-old infants bifidobacteria predominates followed by *Bacteroides*, enterobacteria and enterococci.

At 2 years the microbiota resembles that of adults [13]. However, it has been reported that children (16 months to 7 years) still harbor higher levels of bifidobacteria and enterobacteria than adults [15, 17]. A compilation of data in figure 2 describes some of the microbiota changes between 6 months and 2 years of age.
Characteristics of the Microbiota

The succession and development of microbiota may also influence other parameters related to health. Before weaning there are differences between breastfed and formula-fed infants in the ability to ferment complex carbohydrates, being higher in formula-fed infants probably due to the presence of a more complex microbiota. Following weaning these differences disappear due to an increase in the ability of microbiota to ferment such carbohydrates in the breastfed [18]. In addition, in breastfed infants the establishment of a mucin-degrading microbiota starts later, but in both groups there is an increase in such activity between 6 and 9 months [19]. Also the conversion of cholesterol to coprostanol is initiated during the second half of the first year and it is likely to be dependent on the development of microbiota [20].

Ammonia and phenol concentrations in feces as well as β-glucosidase and β-glucuronidase activities increase after weaning, and even when higher ammonia content and β-glucuronidase activity were found in formula-fed infants, these differences disappear [21].

Creating Mature Microbiota

Following weaning the healthy microbiota, identified as the normal microbiota of an individual that both preserves and promotes well-being and absence of disease especially in the gastrointestinal tract, will gradually be created. Small differences can be reflected in later life and health as shown by studies on microbiota deviations [9, 12, 22].
In the gastrointestinal tract there is a constant challenge by diverse antigens such as microbial antigens, foods and allergens. Such priming of gut-associated lymphoid tissue is important for two opposing functions: mounting a response to pathogens, and maintaining hyporesponsiveness to innocuous antigens. An important question is how the inflammation is kept under control during weaning and how the microbiota is altered during the adaptive process. The strains of the healthy gut microbiota are likely to provide the host with an anti-inflammatory stimulus directing the host–microbe interaction towards a healthy gut [4, 5, 23].

Importantly, the host–microbe cross-talk during and after breastfeeding seems optimal for this target. At this stage the bifidobacteria-dominated environment may provide the child more anti-inflammatory stimuli than bacteria from adults which have been shown to be more proinflammatory [23].

Components of the human intestinal microbiota or organisms entering the intestine may have harmful or beneficial effects on human health, but a complex and diverse community is required for the individual balance. Abundant evidence exists to document that specific strains of the healthy gut microbiota exhibit powerful anti-pathogenic and anti-inflammatory capabilities, and are consequently involved in enhanced colonization resistance in the intestine [24, 25].

**Maintenance of the Individually Optimized Healthy Microbiota**

Creating a healthy gut microbiota during early life must be followed by proper maintenance and enhancement of the individual balance. During times of disease or following detectable deviations in the initial microbiota development, later maintenance can be achieved by directing the gut microbiota into healthy balance by dietary means, for instance by using probiotics or prebiotics. Probiotics are defined as viable microbes which, through oral administration, produce health benefits to the host [24]. Probiotics are members of the healthy gut microbiota and assist in mimicking the healthy microbiota of both a breastfed infant and healthy infant. Prebiotics act through promotion of specific microbes with the potential to maintain health. The prerequisite of this activity is that such strains are already available for the stimulation in the gut. Each bacterial strain and prebiotic substance has its specific effects which have to be evaluated prior to application.

In a like manner, prebiotic oligosaccharides have different microbiota-modifying properties [24]. Probiotics introduce new microbes to the gastrointestinal tract to enhance microbiota maintenance and modification while most prebiotic components have been shown to enhance the *Bifidobacterium* microbiota, which should be defined more clearly. First, the bifidogenic change alone is not a prebiotic effect. Second, the desired *Bifidobacterium* strains should be present in the infant gut for the prebiotic
effect. Third, a clinical benefit has to be documented before a prebiotic effect can be verified.

It has been reported that some fructo-oligosaccharides enhance the levels of unknown microbes in human gut thus potentially facilitating untoward effects. Galacto-oligosaccharides in general are found in breast milk in a great variety, and they have bifidogenic effects and a health-promoting impact on the infant gut. Other than breast milk oligosaccharides, more specific prebiotics with known microbiota and health effects should be developed. Perhaps, as indicated by the mother–infant relationship of offering both microbes and oligosaccharides for the newborn infant, carefully designed combinations of probiotics and prebiotics may offer optimal means for creating and maintaining a healthy microbiota [25].

**Conclusion**

The healthy human microbiota is metabolically active and acts as a defense mechanism for our body. Deviations in its composition are related to multiple disease states within the intestine but also beyond the gastrointestinal tract. Examples of such deviations are given in table 1. Components of the human

---

**Table 1.** Characteristics of infant microbiota: deviations related to atopic diseases

<table>
<thead>
<tr>
<th>Subject group</th>
<th>Before weaning (age 5–6 months)</th>
<th>After weaning (age 6–9 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly sensitized infants, no supplementation</td>
<td>High concentration of <em>Bacteroides</em> and <em>Lactobacillus/Enterococcus</em></td>
<td>Increased <em>Bacteroides</em> and <em>E. coli</em> numbers</td>
</tr>
<tr>
<td>Sensitized infants</td>
<td>Lower levels of <em>Lactobacillus/Enterococcus</em></td>
<td>Lower levels of <em>Lactobacillus/Enterococcus</em></td>
</tr>
<tr>
<td>Highly sensitized infants with bifidobacterial supplementation</td>
<td>High concentration of <em>Bacteroides</em> and <em>Lactobacillus/Enterococcus</em></td>
<td>Decreased <em>Bacteroides</em> and <em>E. coli</em> levels, stabilization of microbiota</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Microbiota at 12 months</th>
<th>Microbiota at 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheezing infants</td>
<td>High <em>Clostridium</em></td>
</tr>
<tr>
<td>Allergic infants</td>
<td>At 6 months lower bifidobacteria and higher clostridia</td>
</tr>
<tr>
<td>Normal infants</td>
<td>At 6 months high bifidobacteria, low clostridia</td>
</tr>
</tbody>
</table>
intestinal microbiota or organisms entering the intestine may have both harmful or beneficial effects on human health.

The available information focuses mostly on the crucial role of infant microbiota and the first colonization steps to later health. Especially bifidobacteria play a key role in this process. The mother–infant contact has an important impact on initial development. The mother provides the first inoculum at birth, promotes the bifidogenic environment through prebiotic galacto-oligosaccharides in breast milk and introduces environmental bacteria through her skin and other contact with the infant thus providing the means to promote guidance to the development of individually optimized microbiota under the existing environmental conditions for each infant.

The future target is to further clarify both the sequelae and the succession of microbial communities especially during and after weaning and during the first years of life. Another target is to understand the use of specific probiotics and prebiotics to influence microbiota development and maintenance as well as dietary management of reported health-related microbiota deviations.

References

Discussion

Dr. H. Hoekstra: Thank you for this wonderful presentation. You talked about windows of opportunity for colonization. I suggest that we split up the discussion on development of the normal microbiota in the first place and then talk about possible interventions. Recently Martin et al. [1] published an article on lactic acid bacteria with probiotic properties present in human milk and on the mammary areola. Could you comment on that study?

Dr. Salminen: I have actually tried to look at that question, and when reading the article itself and looking at the isolation procedures, my first thought is that it is probably skin bacteria. However, there is a Spanish group that has hypothesized that some bacteria might be translocating from the gut to be excreted in breast milk, but I don't have any convincing evidence on that myself. So until I am proven wrong in this, I still consider them as bacteria originating from the skin. I have great difficulties in seeing how the bacteria would be excreted by the mammary gland itself.

Dr. Kleinman: You mentioned how important it is to have a balance of bacteria in the intestine and most of the focus has been on the beneficial effects of the bifidobacteria, but are there any beneficial effects from the so-called detrimental bacteria. Why are they present?

Dr. Salminen: I find it very difficult to attribute the beneficial effect to specific bacteria because even if we introduce a probiotic into the gastrointestinal tract we change the community in the intestinal contents, or perhaps not the community but the metabolic activity of the community. We may not be changing the community at the mucosal level. The other factor that I consider really difficult in research today is that most of our data are based on fecal studies, fecal recovery of probiotic bacteria, fecal concentrations of different bacteria, we really don't know what exactly is happening in the upper parts of the intestine. So I don't find it possible yet to attribute the
health effects or the harmful effects to certain groups of bacteria. Rather we could perhaps identify some bacterial groups or members of the microbiota as biomarkers of changes.

_Dr. Kleinman:_ I am thinking about some of the work, which may have now been discredited, in which there is cross-reactivity for potential pathogens like influenza, for example, and _Escherichia coli_. Has that progressed, do we understand that a bit better now?

_Dr. Salminen:_ Yes, that is a good point. It will certainly provide us more information also from the upper intestinal tract.

_Dr. Rijntjes:_ I have a question concerning colonization in the atopic mother. Is there any difference in colonization if the mother is or is not atopic, or if she has a food allergy or atopic dermatitis?

_Dr. Salminen:_ That is an excellent question that I hope to be able to answer in a year's time. Together with our Japanese colleagues we are actually analyzing that type of set up, how the microbiota is transferred, but I don't have any information available yet unfortunately. Certainly this is an intriguing question since there are genetic and environmental factors together.

_Dr. El-Din Amry:_ Based on the available data, can we define the character of the infant with ideal microflora, the character of the mother, her feeding, mode of delivery, and so on?

_Dr. Salminen:_ That is also a very good question. A couple of years ago, some of you may have even been involved, the European Union funded a 3-year program trying to identify what is average healthy European gut microbiota. I think an interesting result was that there is no such thing as healthy European gut microbiota because it varies so much and we have to look at the individual circumstances. If you really consider nature, the mother has already somehow adapted to the local conditions and is probably trying to transfer protection (against the threats that are in the immediate surroundings) by bacteria transferred at birth, and also by perhaps the specific antibodies in breast milk and the composition of the breast milk. So I don't think we can really identify a sort of common healthy gut microbiota for infants, not to speak about adults, it depends so much on the local conditions.

_Dr. M. Hoekstra:_ When we study colonization of the intestine, we often take stool samples. To what extent does a stool sample reflect what is happening in different parts of the intestine?

_Dr. Salminen:_ Another excellent question to look at the real problem as I see it. Microbiologists have studied stool samples, as discussed earlier; the fecal recovery of different microbes that perhaps reflects the very last part of the colon but not much else. There are recent studies from probiotic interventions but if we look at the oral intake of probiotics in infants, let me say more so in adults, fecal recovery usually disappears within 1–2 weeks. However, if we take biopsies, which is unfortunately most often not possible in infants, from adult volunteers, we can see material in the colon, even in the upper part of the colon. The mucosal biopsies contain large amounts of probiotic bacteria up to 3 months after any signs of fecal recovery. So fecal counts or fecal recovery do not really reflect what is important. But that is a personal opinion and some of you might challenge me on that. I am certain that we need new ways of sampling the upper part of the intestine.

_Dr. M. Hoekstra:_ But I can imagine that you can do animal experiments and catch the stools, and on the other hand take samples from the intestine and see whether they match or not?

_Dr. Salminen:_ You can do animal experiments, yes I agree, especially the very elegant one that was presented by the St Louis group. Genetically defined germ-free animals were chosen for the study. It is also very challenging because the animals were

Gut Microbiota in Infants between 6 and 24 Months of Age
given human microbiota, and then questions were asked such as which humans, from where. We could probably learn the mechanism, but it is a great challenge for us to presently understand the meaning of the study on microbiota actually providing a reservoir assimilating quick storage of fat, but how it varies in different geographic areas, perhaps different nutritional environments, is still completely unknown.

Dr. Aggett: It strikes me though that this model from St Louis really is describing what we understand by colonic salvage. The fat that is being deposited, is that being deposited systemically?

Dr. Salminen: Actually from the study we learned that the microbes that act in the normal microbiota are the ones that rapidly make the carbohydrate part of the diet utilisable, and it was seen as histological differences in the liver and also accumulating fat storage.

Dr. Aggett: But did they look for fatty acid production?

Dr. Salminen: This was the first published experiment describing such a setting and I assume that they did.

Dr. Aggett: And going on from that, would you say something about the proteolytic activity of the colonic bacteria and the relative metabolic growth in that case, and how they may contribute perhaps to colonic salvage and other metabolic phenomena? Additionally do you think that it is possible that such microbial activity could have adverse effects as well as beneficial effects as a result of the systemic absorption?

Dr. Salminen: If I start from the last one, yes I think, as I tried to show in the last slide, we need to know more about the succession of microbes, especially after weaning, because that is where most of us have stopped at the moment. We need to know more about what happens in the upper intestinal tract and by understanding the situation a little bit more carefully it will be possible. I am quite sure there is a possibility of adverse effects and so on. Nature has taken a long time in creating the microbiota as it was perhaps before the war, and we have very rapidly introduced new ways of changing the microbiota by food processing, by sterilizing most of the foods or pasteurizing, or by UHT treatment and by diminishing general microbial exposure. Thus if we had the possibility of comparing intestinal samples from let’s say 100 years ago and now, the diversity would be greater in the old samples. We are doing our best to influence the diversity and to kill all bacteria, and that probably has the greatest influence. Why do we do this? I think there is an excellent example from an American study. It is not comparable but the idea is that if you have cheese made from very clean pasteurized sterilized milk and compare it to the same cheese made from natural milk, the one made from the clean ingredients, sterile ingredients, spoils much faster and probably it is the competition of the microbes in the cheese. Again the diversity is smaller whereas in natural cheese it is greater, and somehow that creates an environment that is more stable. If you have seen the study, similar things could be considered also when we look at intestinal microbiota.

Dr. Waterland: In your list of factors influencing the gut microbiota in infants, I don’t think you mentioned antibiotics.

Dr. Salminen: That is one way of trying to diminish the diversity. That is certainly one of the great impact phases, especially during early childhood, if we look at the use of antibiotics. Even looking at fecal recovery it takes 2–3 months to get back to the normal situation in the microbiota and probably longer, and we may be reintroducing the next antibiotic before the changes have returned to normal.

Dr. Michaelsen: I think that the data on the difference in microbiota and the risk of allergy between infants born by cesarean delivery and vaginal delivery are very fascinating. Don’t you think we know enough to try to do something to help the infant that is born by cesarean section? Shouldn’t we think about a transplant of the maternal microbiota?
Dr. Salminen: I think there are far too few studies available, but as we also have to look at the long-term effects of whatever intervention is done, we can probably point in the right direction. But I don't know what would be a good way.

Dr. Michaelsen: There are a few practical ways to do it.

Dr. Salminen: It would be interesting if there are ways of introducing the cesarean born to the mother's microbiota. It might not be a bad idea, as a matter of fact that is the approach used for chickens; commercial chickens are introduced to their parents.

Dr. Michaelsen: I think it would be reasonable to do it to all infants delivered by cesarean section as well.

Dr. Salminen: Certainly in chickens it has proven to be an effective way of reducing the risk of infections.

Dr. Hardiono Djoened: Is it better to give probiotics as a food supplement or to give it as an infant formula? How do we know whether the dose is right or the type is right?

Dr. Salminen: That is also a good question. Do we know that the dose is right if we use probiotics for instance in infant formula? It is very difficult to estimate the right dose. Today what we use for those estimates is fecal recovery. How much do you need to actually introduce enough into the intestinal tract to provide reasonable fecal recovery which would, in terms of bifidobacteria, be comparable to something that you would see in the normally born infant during the same time? Based on those estimations and very few dose-response studies, I think those have set the basis for the doses used in infant formula today. Of course at the moment we have certainly selected the strains that are the safest possible ones, which have the longest history of use also in other types of foods, trying to be sure that no long-term harmful effects are there. There are a lot of candidate probiotics which have not been introduced because we don't know enough about the long-term effects.

Dr. Bee Wah Lee: If we believe that balance and diversity is important, how does giving a single species of probiotic help in the prevention and treatment of allergic disease or infection?

Dr. Salminen: That is a very important thing to consider. I think there are two totally different options. If we think about all of us here in the room, it would be very difficult indeed to have a single probiotic that would actually change anything in us. Our diversity and complexity is already so well established that something more would probably be needed. But when one considers an infant of less than 1 year of age, maybe less than 6 months old, today we are actually giving them either lactic acid bacteria, which have been shown to specifically promote bifidobacterial microbiota in the intestine, or we give them the same types of bifidobacteria that are part of a normal microbiota. So if the early phase of life actually indicates that we have 60–90% of bifidobacteria, we are certainly promoting that part, but for later purposes we would probably need a combination or different probiotics.

Dr. H. Hoekstra: We haven't talked about the end products of fermentation. Most of the bacteria are involved in fermentation processes and produce different short-chain fatty acids. Do you have data on how to influence the type of short-chain fatty acids that will be formed? For instance, the newborn has a lactate-producing flora while the microbiota of an older child will produce butyrate. Can we influence these processes and would that be important?

Dr. Salminen: This is one of the hot topics of research today. We know that we can influence it to some degree, but rather than influencing that single component I think the issue has been whether we can change the metabolic activity in such a way that the total microbiota handles, let's say, proteins and carbohydrates in a different way. For instance there are ways of reducing the types of metabolic activity which are related to specific clostridia by giving probiotics, but again a community that could change the whole metabolic activity or the effect is very minor.
**Dr. Paerregaard:** I wanted to comment on the possibility of adverse effects of the probiotics. We were discussing that before, when dealing with inflammatory bowel disease, there are data to indicate that probiotics might be beneficial in mild ulcerative colitis and in pouchitis, but also that probiotics may not be efficacious in Crohn's disease. Actually in a large prophylactic study of lactobacillus GG the treatment group became worse than the placebo-treated group. Do you think this would most likely be due to the wrong strain being chosen; could other probiotic strains have been beneficial, or are there specific diseases that definitely should not be treated by probiotic intervention?

**Dr. Salminen:** It is a very complicated question to answer but I will try to tackle it the other way around. We have always tried to consider that if you can identify a deviation in the microbiota, this would relate to whatever disease state or aberrance you are talking about, then you can actually try to find the right strains, even the right species, for correcting that deviation. I would say that specific probiotics could be used for future purposes when we know that there is a problem in the microbiota, if the problem has been identified as much as possible, then try to find the strain or the species that counteracts the problem. Many of the clinical trials have been done that way by picking up something and trying, but without any further basis on the mechanistic side or on the gut microbiota side. I am sure that in this way we will get a lot of negative results, not necessarily due to the probiotic itself or the strain itself but rather by applying it to the wrong purpose at the wrong time perhaps. If we learn more about the microbiota we can also facilitate clinical trials in which a purpose is targeted in the microbiota and then we have the right selection of strains, because I have not seen a wonder strain. Every producer of probiotics likes to say that their strain is good for everything and that is certainly not true as most of you know.

**Dr. Badr-Eldin:** Would it be reasonable to use prebiotics rather than probiotics to try for example to enhance or increase the availability or bioavailability of certain probiotics? I mean using the prebiotics rather than the probiotics.

**Dr. Salminen:** There is a lot of debate today about probiotics and prebiotics and I am sure they have to be handled on a case-to-case basis. My gut feeling is that prebiotics worry me a little bit. We have clearly identified some of the problems in those children who later seem to get atopic diseases and have found biomarkers for them. If we do add a prebiotic to that population, we are not adding anything new, no new microbes, rather we are trying to enhance the microbes that are already there. Then I ask myself the question, are we actually enhancing the problem? Of course prebiotics can change the metabolic activity so that it does not necessarily do what I just described, but I think by introducing something which is familiar for the gastrointestinal tract but not existing at the moment and metabolically active, I would be more prone to look at the probiotic side but certainly on a case-to-case basis. In adults especially it is a totally different game because we might need them both to be able to change something that is established and stable.

**Dr. Schmitz:** Your lecture was planned at the start of this session because, in the idea of the organizers, there is some kind of link between the normal bacterial colonization of the gut and the diversification of foods, and the possibility that toddler's diarrhea might, in some cases, be due to an inadequacy between the food given and the way bacteria were handling it. In one of your graphs where the populations of bacteria are listed from 6 months to 2 years, the curves are very flat as if the big changes in the food ingested and, particularly, the introduction of vegetables and fibers didn't make any change here. How do you see the reaction of the colonic flora to this high input of fibers which are very special for the colon?

**Dr. Salminen:** Unfortunately I have to answer that most of the curves were flat but there was one that was growing and that was the unculturables, the unknowns, and
Gut Microbiota in Infants between 6 and 24 Months of Age

I am sure they do have an effect. There are two factors that should be taken into account. In studies by Dr. Isolauri on rotavirus diarrhea in daycare children, we actually identified that again there is a species composition difference in bifidobacteria. So there may be biomarkers for some subjects who are more prone to diarrheal diseases. But then we have to take into account the rapidly growing unculturable microbiota at that age.

Dr. H. Hoekstra: I think the last question of Dr. Schmitz is a very nice start for the next two presentations.

References