Review

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Human Microbiome

Development of intestinal microbiota in infants and its impact on health

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Throughout the human lifetime, the intestinal microbiota performs vital functions, such as barrier function, metabolic reactions, trophic effects, and maturation of the host's innate and adaptive immune responses. Development of the intestinal microbiota in infants is characterized by rapid and large changes in microbial abundance, diversity, and composition. These changes are influenced by medical, cultural, and environmental factors such as mode of delivery, diet, familial environment, diseases, and therapies used. Thus, it is nearly impossible to define a universal standard for intestinal colonization and development of the intestinal microbiota. This review discusses recent data on the early colonization of the gut by microbial species, development of the intestinal microbiota, and its impact on health.

The human gut microbiota

The largest microbial community of the human microbiome is located in the digestive tract, and more precisely in the large intestine. It is estimated to harbor approximately 10^{14} bacterial cells and more than a 100 times the number of genes of the human genome [1,2]. As such, it plays a very important part in the host's life, being closely interconnected to its health. Over the past 10 years, the massive use of molecular microbiology techniques has contributed to the knowledge about the development of the intestinal microbiota of infants to a level that was impossible to achieve with classic culture techniques, as only 25% of the bacteria from this ecosystem have been cultured to date [3]. Large programs such as the Human Microbiome Project are investigating the diversity of the bacterial population associated with the human body, its inter- and intra-personal variability, the influence of endogenous and exogenous factors, and characterizing its principal constituents (Box 1) [4,5]. Although many of its characteristics are still to be unveiled, most authors agree that the human gut microbiota of a healthy adult is highly resilient and very stable over time, slightly fluctuating on both sides of an equilibrium (homeostasis, Box 2) which is host specific [6,7].

However, before it reaches maturity, the microbiota must develop itself from birth and establish its mutually beneficial cohabitation with the host. Our knowledge of the development of the microbiota in infants has greatly benefited from the latest technologies in molecular microbiology. Precise variations of important bacterial groups (such as *Bifidobacterium*, *Enterobacteriaceae*, *Firmicutes*, and *Bacteroidetes*) can be monitored by quantitative PCR (qPCR), and a much more complete phylogenetic map of the microbiota can be drawn owing to next-generation sequencing (see, e.g., [8]). However, some technical factors such as the choice of PCR primers or the method of bacterial DNA extraction can greatly influence the final results of culture-independent methods [9]. The state of the intestinal microbiota of the patient could be a relevant factor for the design of personalized therapies, and there is an urgent need to clarify the features of all these newly understood elements of the gut microbiota. The aim of this review is to summarize our knowledge of the early development of the intestinal microbiota taking into account environmental factors such as prenatal parameters, the influence of the mother and her microbiota, and therapies occurring around the time of birth. Finally, the current hypothesis of correlations between the development of the gut microbiota, particular types of perturbations, and later occurrence of diseases will be discussed.

Prenatal influences on the development of the gut microbiota

Although it is commonly accepted that the intrauterine environment and newborn infant are sterile until delivery, some evidence shows the presence of bacteria in the intrauterine environment and suggests that these bacteria may influence the microbiota of the infant before birth [10–14]. Bacteria in the intrauterine environment could result in prenatal colonization of the meconium [15]. The presence of bacterial species in the meconium (such as *Escherichia coli*, *Enterococcus faecium*, and

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Box 1. Adult intestinal microbiota

Currently, there is no consensus on the composition of a 'healthy' or 'normal' intestinal microbiota in human adults. However, numerous recent studies have brought some light upon the subject. The two main phyla that are present in the gut are the *Firmicutes* (mainly represented by the genera *Clostridium*, *Faecalibacterium*, *Blautia*, *Ruminococcus*, and *Lactobacillus*) and the *Bacteroidetes* (*Bacteroides* and *Prevotella*) [70]. Other phylas such as *Actinobacteria* (*Bifidobacterium*), *Proteobacteria* (*Gammaproteobacteria* with *Enterobacteriaceae*), or *Verrucomicrobia* (*Akkermansia*) may be underrepresented in numbers but have a major impact on health [71,72]. Among this very broad core microbiota there is room for numerous variations in proportions, diversity, species, and genes functions [73]. However, some recent evidence suggests that despite this high diversity, the main microbial genetic functions could be preserved in almost every individual [1,74]. One of the most studied parameters is the *Firmicutes/Bacteroidetes* ratio and its variations between individuals having a rich Western-type diet or a more rural and vegetable-based diet [8]. Interestingly, this ratio is also tightly linked to obesity and metabolic disorders [75,76]. These phylogenetic variations probably originate from the initial development of the microbiota, and continue throughout the entire life of the individual [77].

Box 2. Gut microbiota homeostasis: definition

In a biological context, homeostasis is a state where a system (cell, organ, organism, or ecosystem) maintains a relative equilibrium of its internal parameters through constant adjustments. When specifically applied to the gut microbiota, it refers to the property of this ecosystem to maintain a balance between the different bacterial groups, the epithelial tissue of the intestine, and the immune system of the host over a period of time. The control parameters are nutrient intake, microbial cell growth, microbial quorum sensing, epithelial tissue regeneration, and immune responses. Dysbiosis is observed when one or more of the control parameters are disturbed, causing a shift in the microbial groups. Disturbances can arise from multiple causes such as xenobiotics (i.e., antibiotics or anticancer drugs), immune imbalance (i.e., inflammatory bowel syndrome), stress, or changes in nutrient intake. Without better knowledge of the complex relationship between the host and its microbiota, dysbiosis is commonly associated with pathological states: obesity, colitis, Crohn's disease, and diarrhea.

Staphylococcus epidermidis) could result from the translocation of the mother's gut bacteria via the bloodstream [10]. In fact, *Enterococcus*, *Streptococcus*, *Staphylococcus*, and *Propionibacterium* species have been isolated from umbilical cord blood, suggesting translocation. In a mouse model, *E. faecium* strains orally fed to the mother were later detected in the amniotic fluid [11]. *Lactobacillus* and *Bifidobacterium* DNA were detected in the placenta of vaginally and cesarean section delivered infants, but no viable cells could be cultivated, suggesting transfer from the gut of the mother [16]. In the amniotic fluid of preterm women with intact membranes, the presence of microbes (bacteria or fungi) was detected by qPCR or culture in 15% of patients [12]. However, there is a delay before the meconium can be harvested (up to several days after birth), and this is more than enough time for the mother's commensal flora (from the vagina or the skin) to travel to the infant's gut and establish supremacy, suggesting a very early rather than prenatal colonization. Moreover, the presence of bacteria in the amniotic fluid could be an indication of an undetected infection and increases the risk of preterm labor [12]. These results raise more questions than they answer. It is still unknown if this presence of bacteria in the intrauterine environment is systematic or exceptional, whether these bacteria are viable and capable of colonizing the infant's gut, and what influence they can have on later stages of the development of the infant's gut microbiota. It is unclear whether colonization of the infant's gut starts with prenatal growth, which is being actively debated, and more studies are needed to correctly understand this phenomenon.

External factors during pregnancy such as drugs, illness, stress, or heavy metal exposure are known to influence the future development and behavior of the infant. Few studies have been conducted so far to determine the impact of these factors on the microbial gut colonization of the infant. In animal trials, infant monkeys born from mothers stressed during pregnancy had significantly lower counts of *Bifidobacterium* and *Lactobacillus* when compared with control infants, born from non-stressed mothers [17]. A study on a large cohort of human infants at 1 month of age showed that the use of antibiotics and/or probiotics by pregnant mothers had no effect on the fecal microbiota of infants, as revealed by qPCR [13]. However, probiotic administration (*Lactobacillus rhamnosus* GG) to mothers during late pregnancy resulted in increased fecal *Bifidobacterium longum* counts in their infants [18]. Overall, it seems that external factors can influence the establishment of the intestinal microbiota of infants, although at a low level (Figure 1). More work is needed to determine if prenatal influences can be overcome by colonization events during the first days of life or not.

Normal development of the infant's intestinal microbiota

The intestinal microbiota of infants is very different from the one of adults and shows very important interindividual variability. Similarities appear around 1 year of age and converge towards a more commonly shared adult-like microbiota [19].

Although it is still very difficult to define a 'normal' human gut microbiota [20], general trends can be inferred from previous studies. The classical pattern of gut microbiota development in infants involves early colonization by facultative anaerobes such as *E. coli* and other *Enterobacteriaceae* [10]. When these organisms have depleted the initial oxygen supplies (in a matter of days), the gut becomes an anaerobic environment, favoring the development of strictly anaerobic bacteria such as *Bifidobacterium*, *Clostridium*, and *Bacteroides*, and sometimes *Ruminococcus*. From an initial low diversity and low complexity, the intestinal microbiota of the infant will slowly develop and mature, reaching an adult state around 3 years of age.

Bifidobacterium is a dominant bacterial genus in the infant gut microbiota [21,22]. Identification of *Bifidobacterium* isolates from the feces of 15 young infants (from day 8 to day 42) revealed the presence of six different species: *Bifidobacterium breve*, *Bifidobacterium longum*, *Bifidobacterium adolescentis*, *Bifidobacterium pseudocatenulatum*, *Bifidobacterium bifidum*, and *Bifidobacterium dentium*, with *B. breve* and *B. longum* being the most prevalent [23]. Several culture-based or culture-independent studies of European and Australian infants revealed *B. breve*,

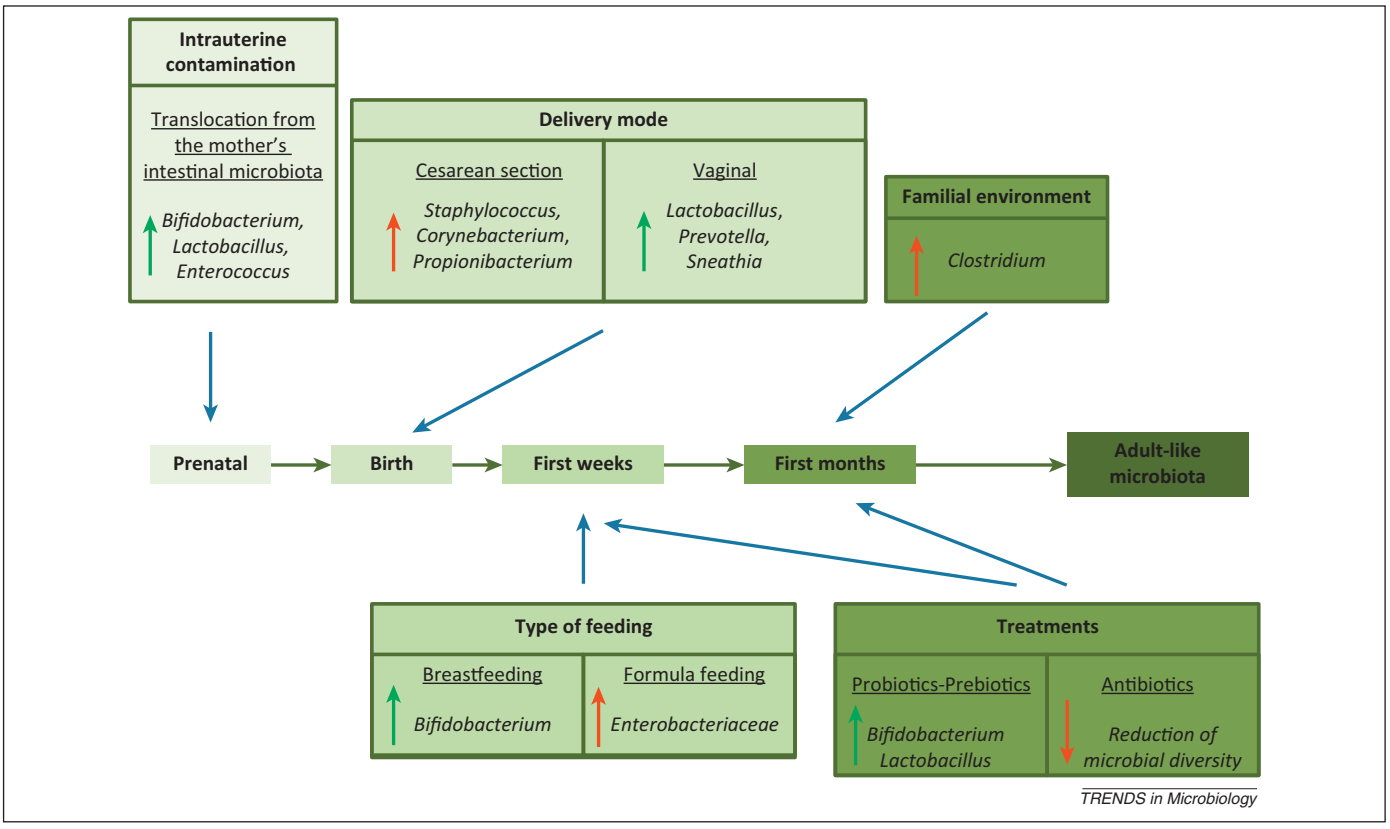

Figure 1. Impact of external factors on the intestinal microbiota of the infant. Green arrows show beneficial modification; red arrows show modification considered negative for healthy development.

B. bifidum, and *B. longum* as the dominant species [18,22,24,25]. Pulsed field gel electrophoresis typing of some of these strains revealed inter- and intra-individual variations in genotypes over time. This suggests that contrary to adults, the *Bifidobacterium* population in the infant microbiota is not stable and can vary rapidly. qPCR analysis of the fecal microbiota of Swedish infants at 1 week of age confirmed the high prevalence of *Bifidobacterium* species, specifically with the supremacy of *B. longum* and *B. adolescentis* [26]. Despite *B. longum* being classically described as typical of the adult gut microbiota [27], recent evidence based on culture-independent techniques have demonstrated the high prevalence of this species in the infant [18,22–24,28,29].

Gestation time is a strong factor that deeply influences the subsequent establishment of the infant intestinal microbiota. Comparison of the fecal microbiota of full-term and preterm infants revealed significant differences. *Enterobacteriaceae* and other potentially pathogenic bacteria such as *Clostridium difficile* or *Klebsiella pneumoniae* were found in greater numbers in preterm infants [28]. In full-term infants, the diversity of the fecal microbiota was higher and more common genera such as *Bifidobacterium*, *Lactobacillus*, and *Streptococcus* were present [30].

Interindividual similarity of fecal microbiota profiles assessed by denaturing gradient gel electrophoresis (DGGE) was significantly higher in preterm infants when compared with full-term babies, indicating the acquisition of a specific hospital-related microbiota [31]. In this study, the prevalence of facultative anaerobic bacteria such as *E. coli*, *Enterococcus* sp., and *Klebsiella pneumoniae* was higher in preterm infants [31].

The succession of bacterial species in the first months of life is very complex. It involves many transient species that will disappear once the conditions of the gut have changed, but also species that will be present during the adult life. Although the time frame and bacterial species involved in the normal development of the intestinal flora of the infant is fairly well understood, the parameters influencing it are more difficult to comprehend [32].

Extrinsic influences on gut colonization in the infant

Influence of the mother

The mother probably represents the most influential external factor for the development of the infant's microbiome, due to intimate contacts during birth, nursing, and early feeding. The influence of the mother on the infant's microbiome can be clearly witnessed during the 1st year of life of the infant. At 1 month of age, the intestinal microbiota of an infant is both functionally and phylogenetically very close to its mother's, as revealed by shotgun sequencing. However, at 11 months significant phylogenetic differences appears while microbiota gene functions remain very close between mother and child [33]. Strong mother–infant association was found by qPCR analysis of the fecal microbiota in the first 6 months after delivery, and was mainly correlated with the presence of *B. bifidum*, *B. breve*, and *Staphylococcus aureus* [34].

Mode of delivery (vaginally or by cesarean section) has been demonstrated to have a strong influence on early gut colonization particularly on the number of *Bifidobacterium*

[35,36]. Analysis of the meconium of newborn infants by pyrosequencing revealed a strong correlation between the first microbial communities of the digestive tract and the microbial communities of either the mother's vagina (*Lactobacillus*, *Prevotella*, or *Sneathia*) in the case of vaginal delivery or the mother's skin (*Staphylococcus*, *Corynebacterium*, and *Propionibacterium*) in the case of cesarean section [37]. Moreover, temporal temperature gradient gel electrophoresis (TTGE) and DGGE analysis of fecal samples 3 days after birth revealed differences between cesarean and vaginally delivered infants. *Bifidobacterium* numbers were significantly lower in cesarean born children, and the overall diversity of their microbiota appeared to be lower [38]. This evidence demonstrates that the gut environment becomes populated by the first abundant microbial communities it encounters, either the skin or the vaginal environment. However, in preterm infants the delivery mode seems to have less influence on the gut colonization: analysis of fecal samples by classical or culture-independent methods of preterm infants revealed no correlation between delivery mode and the colonization levels of various microorganisms, including *Bifidobacterium* [30]. In the same way, meconium analysis using 454 pyrosequencing of six preterm infants with very low birth weight showed strong colonization by *Staphylococcus* species for three subjects, two born by cesarean section and one born vaginally [15]. In the long term, a significant increase in clostridia has been described in 7-year-old children born vaginally compared with cesarean delivered children. However, no other differences were reported in bifidobacteria, lactobacilli, or *Bacteroides* numbers [39]. The unique characteristic of this last study illustrates the need for more data on the long-term influence of the first microbiota to colonize the infant gut.

Apart from the delivery mode, another strong influence in the development of the infant intestinal microbiota is the mode of feeding. Plate counts of breast milk samples revealed the presence of *Streptococcus* and *Staphylococcus* genus, which correspond to early colonizers of the gut [25,40,41]. *Bifidobacterium* and *Lactobacillus* are also frequently detected, suggesting an important role of breast milk as a delivering system for probiotic bacteria [42]. Indeed, breastfed infants show significantly higher counts of *Bifidobacteria* and *Lactobacillus* and lower counts of *Bacteroides*, *Clostridium coccoides* group, *Staphylococcus*, and *Enterobacteriaceae* as compared with formula-fed infants [21,43,44]. Genotyping of bacterial isolates (*Lactobacillus*, *Staphylococcus*, and *Bifidobacterium*) from the breast milk of mothers and fecal samples of their infants revealed the presence of identical strains, suggesting an important role of breast milk as a source of early gut colonization in infants [45]. A case study, following the development of the intestinal microbiota of an infant from his birth to 2.5 years old revealed a strong influence of the diet in the variations of the microbial communities [29]. The human breast milk is an important source of oligosaccharides, which have a strong prebiotic effect for the neonate's developing microbiota [46]. *Bifidobacterium longum* subsp. *infantis* possess several gene clusters dedicated to the metabolism of these human milk oligosaccharides (HMOs) [47]. HMOs also upregulate the expression of several pathways in *B. longum* subsp. *longum*, notably genes involved in carbohydrate degradation and cell adherence [48]. Thus, initial colonizers such as *Firmicutes* and *Actinobacteria* are well suited for the utilization of breast milk, but also possess some genes facilitating the assimilation of non-digestible plant polysaccharides: even before the introduction of solid food, the intestinal microbiota is ready for simple vegetal food such as rice [29,47]. With the introduction of more complex table food and infant formula there is a rapid increase in *Bacteroidetes*, and enrichment in functional genes responsible for carbohydrate and xenobiotic degradation as well as vitamin biosynthesis [29]. Shifts in the community of lactobacilli species have also been reported shortly after weaning [29].

Environmental influences

Apart from the mother, the familial environment has also been described as a strong influencing factor in the development of the intestinal microbiota. For example, infants with older siblings have lower total counts of bacteria per gram of feces, but a comparatively greater proportion of *Bifidobacterium* [13]. All these sources of variation are also strongly influenced by geographical locations and cultural traditions. When comparing the fecal microbiota of children aged 0–3 years from three distinct environments (30 Amerindians from the Amazonas in Venezuela, 31 Malawians from a rural area, and 31 Americans from US urban areas), significant differences in the phylogenetic composition of the microbiota were found. The difference was less pronounced when comparing Amerindians and Malawian children than when comparing these non-Western children with Western (American) children. Despite these differences, *Bifidobacterium* dominated the fecal microbiota of all three groups of children before 1 year of age [8]. In another study, significant differences were recorded between Finnish and German children: Finnish infants had higher prevalence and counts of *Bifidobacterium* than German infants, and lower counts of *Akkermansia muciniphila*, *Clostridium histolyticum*, and *Bacteroides–Prevotella* [24].

Compared with adults, the fecal microbiota of children younger than 3 years old showed a low diversity index. This is even more obvious when only children between 0 and 1 year are taken into account. The maximum number of operational taxonomic units (OTUs) for children between 0 and 1 year is approximately 1000, whereas adults commonly exhibited between 1000 and 2000 OTUs [8]. However, interindividual variations are significantly greater among children than among adults: the microbiota of children is dominated by a few bacterial genera and species, but these dominant groups are highly variable between individuals. These interindividual differences diminish as the microbiota become more complex with age [8]. The mother as well as cultural and geographical factors have a tremendous influence on the development of the intestinal microbiota in infants. The familial environment is a major source of bacteria that will colonize the gut during the first years of life. More studies are needed to determine whether imbalances in the intestinal microbiota and/or microbiota-related diseases (such as colitis, inflammatory bowel disease, or allergies) could be transmitted to a newborn by other members of the household.

Table 1. Main pathologies and antibiotic treatment in neonates

Pathologies	Age (days)	Pathogens	Antibiotic treatment	Treatment duration (days)
Peripartum prophylaxis	Prenatal	Group B streptococcus	Penicillin G, or, if penicillin allergy, cefazolin, clindamycin, or vancomycin	Every 4 h until delivery
Early onset perinatal infection	Before day 8	Group B streptococcus, *Escherichia coli*, *Listeria monocytogenes*	Ampicillin and gentamicin[a]	8–10 days (2 days of aminoglycoside)
Late-onset perinatal infection (commonly bacteremia and meningitis, rarely arthritis or osteomyelitis)	Days 8–80	Group B streptococcus	Ampicillin and gentamicin[a]	1–14 days (2 days of aminoglycoside); 21–28 days in the case of arthritis or osteomyelitis
Nosocomial neonatal infection (commonly catheter-related septicemia or pneumonia, especially in cases of prematurity, intrauterine growth retardation, or congenital malformation)	Days 5–80	Coagulase-negative staphylococci	Probabilistic before documentation	7–10 days
		Staphylococcus aureus	Vancomycin, amikacin, and ceftazidime	
		Pseudomonas aeruginosa (rarely)		
Pneumonia (or surinfected bronchiolitis)	Days 5–80	Group B streptococcus, *Streptococcus pneumoniae*	Ampicillin	10 days
Pyelonephritis	Days 7–80	*Escherichia coli*	Ampicillin and gentamicin	10–15 days

[a]In the case of severity, the probabilistic antibiotic treatment combines a third-generation cephalosporin (cefotaxime) with ampicillin and gentamicin. The antibiotic treatment is secondarily adapted in response to microbiologic documentation.

How treatments affect the infant intestinal microbiota

Contact with the mother, mode of delivery, feeding, and contact with other infants are common to all children, and are considered as part of normal development. However, the intestinal microbiota can also be artificially modified in a way that is specific to some individuals, mainly occurring during the course of illness and treatments (Table 1).

Therapies of the mother or the infant

Most drug-based therapies influence the microbiome of the patient in some way [49]. This is also true for infants, with an additional factor: as we have previously seen, the mother has a tremendous influence on the infant's microbiota, and treatment of the mother can affect the child indirectly.

Antibiotherapy in infants was associated with higher proportions of enterobacteria and enterococci, and lower proportions of bifidobacteria [50]. Some of these differences could still be detected 1 month after the end of treatment. Early antibiotic treatments in very low birth weight neonates also significantly reduced microbial fecal diversity [15] and fecal microbial counts [51]. Antibiotherapy results in changes in the normal development of the intestinal microbiota, generally coinciding with a decrease in phylogenetic diversity [29]. Antibiotherapy of mothers (prenatal or during breastfeeding) was associated with lower proportions of *Bacteroides*, *Atopobium*, and a lower sum of total detected bacteria [43]. Reduction of the phylogenetic diversity in infants should be carefully monitored, as it has been related to the onset of neonatal sepsis [15]. Should these data be confirmed by other studies, it could represent a powerful tool to detect early risks of sepsis in neonates.

Impact of probiotics and prebiotics supplementation on the development of the infant microbiota

As described previously, the succession of different bacterial groups is critical for the maturation of the intestinal microbiota in infants. Among these groups, *Bifidobacterium* and other lactic acid bacteria are viewed as essential and beneficial. Is it possible then to modify the infant's diet in order to favor the implementation of these bacteria? Probiotics are live microorganisms consumed for their beneficial properties. In adults, they colonize the intestine in a transient way and are rarely detected in fecal samples 2 weeks after discontinuation of intake [52]. However in infants, the microbiota is not mature, and the concentration and diversity of bacterial groups may not be sufficient to oppose colonization by a newly introduced member. In this section, we will briefly review the most recent evidence concerning the modulation of the intestinal flora of infants by consumption of probiotics or prebiotics.

Since bacteria are transmitted from the mother to the infant, the consumption of probiotics by the mother could influence the development of the microbiota of their children. The consumption of probiotics by Finnish mothers before delivery and during breastfeeding induced a modulation of the colonization and development of the *Bifidobacterium* flora of their infants, particularly by increasing the diversity of the *Bifidobacterium* species present [53]. However, in another study the infants had lower *Bifidobacterium* counts compared with placebo groups, but significantly higher lactic acid bacteria (*Lactobacillus* and *Enterococcus*) counts [24]. Other combinations of probiotics given to the mother during 2 months before and 2 months after delivery (*L. rhamnosus* + *B. longum* or *Lactobacillus paracasei* + *B. longum*) increased the similarity of the mother–infant microbiota, but showed no significant modification of the colonization rates or *Bifidobacterium* diversity in the infants [34].

The microbiota and immune system are developing rapidly in newborns and safety is a major concern when they are fed with probiotics. A total of 132 infants receiving the probiotic strain *L. rhamnosus* GG during 6 months after birth were followed for 2 years after treatment, showing a good tolerance and no significant changes in the fecal microbiota in the long term [54]. A study on very low birth weight preterm infants showed no improvement of the gastrointestinal tolerance to enteral feeding during

supplementation with *B. longum* BB536 and *L. rhamnosus* GG [55]. Preterm infants receiving a bifidobacteria-enriched formula had significantly higher *Bifidobacterium* counts than the placebo group, but no differences were detected for other bacterial groups including lactobacilli, Gram-negative enteric bacteria, or staphylococci [56].

An infant formula containing a prebiotic (galacto- and long-chain fructooligosaccharides) was well tolerated by infants born at term, leading to somatic growth and tending towards a reduction of the number of clostridia and *E. coli*, while slightly increasing bifidobacteria [57].

Probiotics and prebiotics seem to be well tolerated by infants and their mothers. Reports of secondary effects are scarce, and the homeostasis of the microbiota is preserved for the most part. They have shown beneficial effects in infants for protection against infections [58], diarrhea [59], necrotizing enterocolitis [60], eczema [61], and atopic dermatitis [62]. Therefore, it appears safe to recommend the use of well-known and extensively tested probiotics for the improvement of specific conditions in infants [63].

Long-term effects of specific microbiota colonization

It is becoming evident that initial microbial colonization and the resulting immune and metabolic programming have a long-lasting influence on the risk for diseases. For example, cesarean section delivery seems to increase the risk of celiac disease, type 1 diabetes, and asthma, which is generally associated with excessive or aberrant T-helper responses [64]. Three weeks after birth, the bacterial cellular fatty acid profile in fecal samples differs significantly between infants developing atopy and those not [65]. Furthermore, lower numbers of *Bifidobacterium* during early infancy (6 and 12 months) correlated with being overweight and obesity when infants reached 7 years of age [66].

Concluding remarks

During the first years of life, the intestinal microbiota of infants evolves rapidly until it reaches homeostasis [8]. From this point, the bacterial composition and phylogeny will generally remain very stable over time. It is now commonly accepted that the microbiota influences numerous aspects of the host's metabolism. Despite the fact that most of the causality is not yet fully understood, a strong relationship has been described between variations of the microbiota and disease susceptibility [67].

Some studies have already demonstrated the predictive power of the microbiota in enteric diseases [68]. The next step will be determining whether early variations of the intestinal microbiota in infants can be linked with metabolic or systemic conditions later in life. The first example has been recently proposed, with a retrospective study on a cohort of 11 532 children from the UK demonstrating that infants exposed to antibiotics in the first 6 months of life have a significantly higher body weight than unexposed children [69]. With the multiplication of data, other relationships of this kind are very likely to emerge in the next years. The hope behind this approach is to identify risks factors within the microbiota for concerns such as obesity, diabetes, and allergic diseases, to mention a few examples. It has not yet been demonstrated if interventions aimed at the microbiota (including probiotics, prebiotics, or targeted antibiotics) could help in suppressing these risk factors and increasing the overall health of infants and adults. Huge progress has been made in recent years to understand the dynamics of intestinal microbiota development in infants and the influence of different parameters. The exact relationship between early microbiota variations and adult diseases (such as allergy or obesity) should be investigated further. In return, it would allow the development of new therapeutic approaches based on targeted modification of the microbiota of infants in order to reduce their risk of disease later in life.

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