Revisiones

Immunomodulatory effect of fibres, probiotics and synbiotics in different life-stages

J. Romeo¹, E. Nova¹, J. Wärnberg¹, S. Gómez-Martínez¹, L. E. Díaz Ligia¹ and A. Marcos¹


Abstract

Chronic diseases associated to modern lifestyle habits are usually related to immune system malfunction. In this context, since diet is very well-known to modulate host resistance to infectious and inflammatory processes, the consumption of fibre and probiotics seems to be a promising nutritional tool for immune system modulation in different populations. Health effects of dietary fibres and probiotics have been extensively documented in numerous epidemiological and intervention studies, especially their beneficial effect on intestinal microbiota with important clinical implications in the prevention and/or treatment of infectious and inflammatory diseases. Mechanisms may include modulation of the functional properties of the microbiota, epithelial cells, dendritic cells and immune cell types. Prebiotics have been extensively reported to affect the composition of the gut microbiota, stimulating directly or indirectly putative beneficial gut commensals other than lactic acid bacteria, opening promising areas of research for the discovery of new probiotic strains and synbiotic combinations. Age-related changes in gut physiology, microbiota and mucosal immune response are well established. Moreover, exposure to different challenges during life such as early encounter of environmental insults in the newborn, infant formula feeding, antibiotic treatment, gastrointestinal diseases and stress, also interferes with the normal development and balance of the healthy gut microbiota. Therefore, the current short review gives an overview of today’s main aspects of the effect of fibres, probiotics and synbiotics on the immune system in different life-stages.

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Key words: Immunomodulation. Fibre. Probiotics. Lifespan.

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EFECTO INMUNOMODULADOR DE LA FIBRA, PROBIÓTICOS Y SIMBIÓTICOS EN LAS DIFERENTES ETAPAS DE LA VIDA

Resumen

Las enfermedades crónicas relacionadas con el estilo de vida frecuentemente están asociadas con una alteración del sistema inmunológico. En este sentido, ya que la dieta es capaz de modular la resistencia a infecciones y procesos inflamatorios, el consumo de fibra y probióticos parece ser una herramienta prometedora en la modulación del sistema inmune en diferentes poblaciones. Los efectos saludables de la fibra dietética y los probióticos han sido documentados en numerosos estudios epidemiológicos y de intervención, especialmente sus efectos beneficiosos sobre la microbiota del intestino con implicaciones clínicas importantes en la prevención y/o tratamiento de enfermedades infecciosas e inflamatorias. Los mecanismos incluyen la modulación de las propiedades funcionales de la microbiota, células epiteliales, dendríticas e inmunológicas. Se han estudiado en profundidad cómo los prebióticos afectan a la composición de la microbiota del intestino, estimulando directamente o indirectamente potenciales beneficiosos intestinales no oportunos, modificando la formación de nuevas cepas de probióticos y combinaciones de sinbióticos. Por otro lado, están bien establecidos los cambios en la fisiología del intestino, microbiota y respuesta inmune asociados al envejecimiento y en otros momentos vitales. Además, las agresiones externas en los primeros días de vida, la alimentación con formulas infantiles, el tratamiento con antibióticos, las enfermedades gastrointestinales y el estrés, también alteran el desarrollo y equilibrio de la microbiota intestinal. Por todo ello, esta revisión ofrece una visión actual de los aspectos más relevantes del efecto de la fibra, probióticos y sinbióticos sobre el sistema inmune en las diferentes etapas de la vida.

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Palabras clave: Immunomodulación. Fibra. Probióticos.

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Introduction

Developed societies are facing up to a progressive increase on immune-mediated and gut-related health problems, such as allergies and autoimmune and inflammatory diseases. Recent compelling evidence has suggested that emerging nutritional strategies may contribute to decrease these host-related diseases manipulating the microbiota by diet. In this context, the increased use of prebiotic fibres and probiotics has become a major area of interest within the nutrition community and seems to be a promising nutritional tool to modulate the immune system in different populations. These specific nutrients/ingredients are included into several functional foods that may improve the functions of both the immune system and the gut physiology as well as metabolic functions.

Mechanisms contributing to altered in vivo immune function induced by functional foods may include modulation of the microbiota itself, improved barrier function and direct effects of bacteria on different epithelial and immune cell types (monocytes/macrophages, B cells, T cells and NK cells). The increasing incidence of allergies may be explained by a dysregulation in the T helper (Th1/Th2) balance linked to the modern hygienic lifestyle, but this does not explain the increased incidence of other disorders such as inflammatory bowel diseases, which are all primarily driven by Th1 cells. In this respect some animal studies have suggested that induction of regulatory T cells by certain microorganisms can prevent or alleviate such diseases. In any case, despite the positive clinical effects on the prevention and treatment of several immune-related diseases, the mechanisms of this type of functional foods are still not completely understood.

Age-related physiological changes

Although relatively little work has been done to describe the gastrointestinal changes associated with normal aging in humans, age-related changes in gut physiology, microflora and mucosal immune response are well established. Exposure to different challenges during life such as early encounter of environmental insults in the newborn, infant formula feeding, antibiotic treatment, gastrointestinal diseases and stress, interfere with the normal development and balance of the healthy gut microflora.

The pattern of intestinal microflora undergoes major ecologic modifications in the early stages of life. Some authors have suggested that adequate establishment of the intestinal flora after birth plays a crucial role in the development of the innate and adaptive immune system. In fact, infants are highly susceptible to infection during early life, which, in large part, is the result of delayed development of the immune function and changes in the composition and number of gut flora after weaning. The colonization of the human intestine begins at birth and the composition of the intestinal microbiota is influenced by diet composition. Breast feeding constitutes one route for oral delivery of microbes and antigens. In addition, it has been reported that human milk provides molecules with antimicrobial activity as well as probiotic bacteria such as Lactobacillus gasseri and Lactobacillus fermentum.

On the other hand, the activity of the immune system and the development of mucosal immune responses to new antigens decline with age. The number of factors affecting the idiosyncratic immune characteristics of the individual, such as environmental insults, alteration of the microflora, along with the risk of inflammatory diseases, increase with age. For example, numbers of bifidobacteria in the gut decrease markedly after 55-60 years of age. Therefore, prebiotics and probiotics may have a particular interest in this high-risk group, even preventing immune senescence and several age-related diseases.

Prebiotic and probiotic immune protection in infants and children

Prebiotics target indigenous beneficial bacteria already established in the gut and have become relevant in infant nutrition, as formula-fed infants usually have lower numbers of bifidobacteria compared to the breastfed infants. Taking breast-feeding as the natural example of infant nutrition, the prebiotics approach should be considered as a physiological approach to influence intestinal microbiota early in life. In this regard, Bruzese et al. suggested that the addition of non digestible oligosaccharides and inulin to infant food may exert a comparable effect to human milk. Moreover, prebiotics can simulate the bifidogenic effects of breast milk oligosaccharides and have been shown to exert long-term effects (up to two years) for protecting against infection, lowering the incidence of allergy and also exerting positive consequences for the postnatal development of the immune system.

The prebiotic fibres inulin and oligosaccharides have been extensively studied in infants and children. The addition of the inulin/galactooligosaccharides (GOS) mixture in weaning foods of 4- to 6-month-old infants in a daily dose of 4.5 g during 6 wk succeeded in increasing of the faecal percentage of Bifidobacteria population (form 43 to 57%) of the fecal flora. Other intervention study in infants receiving an inulin/GOS mixture during 12 months, significantly decreased the episodes of gastrointestinal and respiratory tract infections, also enhancing faecal immunoglobulin (Ig) A levels. Moreover, inulin and oligofructose have also been reported as promoting positive effects as indicated by a lower incidence of febrile episodes in infants. Regarding oligosaccharides alone, a beneficial effect on the immune system of preterm infants due to the specific conditions in the luminal part of the...
Table I
Summary of studies reporting effects on immunity with prebiotics, probiotics and synbiotics

<table>
<thead>
<tr>
<th>Reference</th>
<th>Design</th>
<th>Population Description</th>
<th>Dose</th>
<th>Prebiotic/Probiotic Dose</th>
<th>Effect on Immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scholtens et al., 2006a</td>
<td>Double-blind, randomised intervention study for 6 weeks</td>
<td>38 infants (4-6 months)</td>
<td>4.5 g/d</td>
<td>Galacto-oligosaccharides (GOS) and fructo-oligosaccharides (FOS) (9:1)</td>
<td>The level of bifidobacteria in the intestinal microbiota increased</td>
</tr>
<tr>
<td>King et al., 2007a</td>
<td>Randomised crossover intervention study for 3 weeks</td>
<td>35 subjects (18 lean normotensive and 17 obese hypertensive individuals) (18-49 years)</td>
<td>30 g/d</td>
<td>Naturally present fibre in diet and supplemented fiber (psyllium)</td>
<td>Reduced levels of CRP in both fibre interventions. Greater reduction in lean normotensive compared with obese hypertensive subjects (49% vs 10%)</td>
</tr>
<tr>
<td>Schiffin et al., 2007a</td>
<td>Prospective, randomized, double-blind, controlled intervention study for 12 weeks</td>
<td>74 elderly subjects (undernourished or at risk of undernutrition)</td>
<td>1.3 g/250 ml/d (daily liquid supplement)</td>
<td>Oligosaccharides (OS)</td>
<td>Decreased levels of pro-inflammatory gene transcription activation (TNF-α mRNA and IL-6 mRNA)</td>
</tr>
<tr>
<td>Ma et al., 2008a</td>
<td>Cross-sectional observational study during 6 years</td>
<td>1958 postmenopausal women</td>
<td>16 g/d of total dietary fibre</td>
<td>Dietary fibre intake by self-report questionnaire</td>
<td>High-fibre diet is associated with lower plasma levels of IL-6 and TNF-α-R2</td>
</tr>
<tr>
<td>Shadid et al., 2007a</td>
<td>Randomized, double-blind, placebo-controlled study from week 25 of gestation until delivery</td>
<td>48 pregnant women</td>
<td>3 g/d (3 times/d)</td>
<td>GOS:FOS (9:1)</td>
<td>Increased bifidobacteria counts only in maternal faecal samples. No effects on children’s immunity</td>
</tr>
<tr>
<td>Vulevic et al., 2008a</td>
<td>Double-blind, placebo-controlled, crossover study for 24 weeks</td>
<td>44 healthy elderly</td>
<td>5.5 g/d</td>
<td>GOS mixture</td>
<td>Increases in phagocytosis, NK cell activity, and IL-10 production. Reduction in the production of IL-6, IL-1β, and TNF-α by mitogen stimulated PBMCs</td>
</tr>
<tr>
<td>Anjarogh et al., 2008a</td>
<td>Prospective, randomized, double-blind, placebo-controlled intervention study for 2 years</td>
<td>134 healthy infants (aged between 37 and 42 weeks)</td>
<td>8 g/L scGOS:kFOS</td>
<td>GOS and FOS</td>
<td>Lower incidence of clinical allergic manifestations and infections until 2 years of life</td>
</tr>
<tr>
<td>Bruzese et al., 2009a</td>
<td>A multicenter, prospective, randomized, placebo-controlled open trial for 12 months</td>
<td>342 healthy infants (mean age 53.7+/−32.1 days)</td>
<td>0.4 g/100 ml/d</td>
<td>GOS:FOS (9:1)</td>
<td>Reduced intestinal and, possibly, respiratory infections in healthy infants during the first year of life</td>
</tr>
<tr>
<td>Lee et al., 2001a</td>
<td>Randomized prospective clinical study</td>
<td>100 children (6-60 months of age) for 4 days</td>
<td>One capsule containing 10^9 viable L. acidophilus (LA) and 10^9 B. infantis</td>
<td>Decreased frequency and duration of diarrhoea during hospitalization</td>
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<tr>
<td>Solis et al., 2002a</td>
<td>Randomized controlled intervention trial</td>
<td>22 children (6 and 24 months) malnourished for 2 months</td>
<td>150 and 200 kcal/kg/day of milk containing probiotics</td>
<td>Lactobacillus acidophilus (LA) Bifidobacterium infantis (BI)</td>
<td>Increased IFN-γ production by PBMC stimulated with yoghurt bacteria</td>
</tr>
<tr>
<td>Naruszewicz et al., 2002a</td>
<td>Randomized, controlled, double blind study for 6 weeks</td>
<td>36 healthy smoker volunteers (18 women and 18 men) (35–45 years)</td>
<td>400 mL/d of probiotic formula</td>
<td>Lactobacillus bulgaricus Streptococcus thermophilus</td>
<td>Decrease in plasma IL-6 concentration (41%)</td>
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<tr>
<td>Reference</td>
<td>Design</td>
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<td>Dose</td>
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<tr>
<td>Rosenfeldt et al., 2003</td>
<td>Double-blind, placebo-controlled, crossover study for 6 weeks</td>
<td>43 children with atopic dermatitis (1-13 years)</td>
<td>10^9 cfu of each strain</td>
<td>Lysophilized <em>Lactobacillus rhamnosus</em> 19070-2 <em>Lactobacillus reuteri</em> DSM 122460</td>
<td>Improved eczema</td>
</tr>
<tr>
<td>Pohjavuori et al., 2004</td>
<td>Randomized, double-blind study design for 4 weeks</td>
<td>119 infants with cow’s milk allergy (age, 1.4-11.5 months; mean, 6.5; 61% boys)</td>
<td>5 x 10^9 cfu LGG MIX group: 5 x 10^9 cfu LGG 5 x 10^9 cfu LC705 2 x 10^9 cfu BBb99 2 x 10^9 cfu PJS</td>
<td><em>Lactobacillus rhamnosus</em> GG (ATCC53103) MIX group: <em>Lactobacillus rhamnosus</em> GG (ATCC53103) <em>Lactobacillus LC705</em> <em>Bifidobacterium breve Bb19</em> <em>Propionibacterium freudenreichii subsp. shermanii JS</em></td>
<td>Increased levels of secreted IFN-γ by mitogen-stimulated PBMC in the LGG group</td>
</tr>
<tr>
<td>Bakker-Zierikzee et al., 2006</td>
<td>Randomized, double-blind intervention study for 32 weeks</td>
<td>57 healthy infants at birth</td>
<td>100 ml/d of prebiotic formula 100 ml/d of probiotic formula</td>
<td>0.6 g GOS/FOS (90:10) /100 ml 6.0 × 10^9 cfu <em>Bifidobacterium animalis</em> /100 ml formula</td>
<td>Higher faecal SIgA levels in the prebiotic group compared with the control</td>
</tr>
<tr>
<td>Nova et al., 2006</td>
<td>Prospective, randomised, controlled and parallel trial for 10 weeks</td>
<td>30 adolescents with anorexia nervosa (13-19 years)</td>
<td>Yogurt (375 g/day) containing probiotics 10^9× 10^9 cfu/ml each</td>
<td><em>Lactobacillus delbrueckii subsp. bulgaricus</em>; <em>Streptococcus thermophilus</em></td>
<td>Higher CD4/CD8 ratio Increased IFN-γ production by PHA stimulated PBMCs</td>
</tr>
<tr>
<td>Passeron et al., 2006</td>
<td>Double-blind prospective randomized study for 3 months</td>
<td>41 children aged at least 2 years with atopic dermatitis</td>
<td>1.2 x 10^9 colony-forming units 3 times per day</td>
<td><em>Lactobacillus rhamnosus</em> Lcr35 plus probiotics (from fermentation broth for <em>L. rhamnosus</em> Lcr35) Prebiotics alone</td>
<td>Improve the manifestations of atopic dermatitis measured by Scoring Atopic Dermatitis (SCORAD) score (both synbiotics and prebiotics interventions used alone)</td>
</tr>
<tr>
<td>Lara-Villoslada et al., 2007</td>
<td>Intervention longitudinal controlled trial for 6 weeks</td>
<td>30 children (3-12 years) with no gastrointestinal pathology</td>
<td>1.8 x 10^9 cfu/L CECT5711 0.2 x 10^9 cfu/L CECT5716</td>
<td><em>Lactococcus garvieae</em> CECT5711</td>
<td>Higher faecal and saliva IgA levels</td>
</tr>
<tr>
<td>Uchiida et al., 2007</td>
<td>Intervention longitudinal controlled trial for 1 year</td>
<td>4 paediatric patients with short bowel syndrome (2-13 years)</td>
<td>3.0 g per day of probiotics (1.0 g of <em>Bifidobacterium breve</em> (BB), <em>Lactobacillus casei</em> (LC) and GOS 3.0 g per day of GOS)</td>
<td><em>Bifidobacterium breve</em> (BB); <em>Lactobacillus casei</em> (LC) and GOS</td>
<td>CD3(+) and CD8(+) T-cells increased</td>
</tr>
<tr>
<td>Hol et al., 2008</td>
<td>Double-blind, randomized, placebo controlled study for 12 months</td>
<td>119 infants with cow’s milk allergy (mean age, 4.2 months; 55% boys)</td>
<td>10^9 cfu formula for each bacteria</td>
<td><em>Lactobacillus casei</em> CRL431 and <em>Bifidobacterium lactis</em> Bb-12</td>
<td>Higher percentages of CD3+ and CD3+CD4+ lymphocytes only in the placebo group</td>
</tr>
<tr>
<td>Kopp et al., 2008</td>
<td>Double-blind, placebo-controlled prospective intervention study from 4 to 6 weeks of gestation until delivery and for 6 months within infants</td>
<td>105 pregnant women from families with &gt; = 1 member (mother, father, or child) with an atopic disease</td>
<td>5 x 10^9 cfu</td>
<td><em>Lactobacillus GG</em></td>
<td>No clinical effects (atopic symptoms, total IgE concentrations, upper respiratory tract infections, fever)</td>
</tr>
</tbody>
</table>
Table I (continuation)

<table>
<thead>
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<tbody>
<tr>
<td>Ivory et al., 2008</td>
<td>Double-blind, placebo-controlled intervention study for 5 months</td>
<td>20 adults with seasonal allergic rhinitis (18-45 years)</td>
<td>6.5x10^9 Le/65 mL probiotic drink</td>
<td>Lactobacillus casei Shirota (LcS)</td>
<td>Levels of antigen-induced IL-5, IL-6 and IFN-γ production decreased</td>
</tr>
<tr>
<td>Loo et al., 2008</td>
<td>Meta-analysis of ten double-blind randomized controlled clinical trials</td>
<td>Paediatric populations</td>
<td></td>
<td>Lactobacillus Bifidobacterium</td>
<td>Probiotics are efficient in prevention of paediatric atopic dermatitis (prenatal and postnatal regimen) for pregnant women</td>
</tr>
<tr>
<td>Manschae et al., 2008</td>
<td>Randomized double-blind placebo-controlled study</td>
<td>98 infants with a family history of allergy for 6 months</td>
<td>5x10^9 cfu (LGG) 5x10^9 cfu (LC705) 2x10^8 cfu (BB99) 2x10^8 (PJS)</td>
<td>Lactobacillus rhamnosus GG (ATCC 53103) L. rhamnosus LC705 Bifidobacterium breve BB99 Propionibacterium freudenreichii sp. Shermani JS</td>
<td>Increased IgE, IgA and IL-10 plasma concentrations</td>
</tr>
<tr>
<td>Prescott et al., 2008</td>
<td>Randomized double-blind, placebo-controlled trial for 6 months</td>
<td>153 children from birth to 6 months</td>
<td>3x10^9 cfu</td>
<td>Lactobacillus LAFTI L10</td>
<td>No significant effect on allergy outcomes (innate responses to toll-like receptor (TLR) function)</td>
</tr>
<tr>
<td>Ogawa et al., 2006</td>
<td>Longitudinal intervention trial for 1 week</td>
<td>8 healthy adults (six males, two females; average age 34.9 years)</td>
<td>1x10^9 cfu of LCC 1g of dextran</td>
<td>L. casei sp. casei (LCC) Dextran</td>
<td>Increase of NK cell activity</td>
</tr>
<tr>
<td>Kukkonen et al., 2007 and 2008</td>
<td>Randomized, double-blind, placebo-controlled study with 2 parallel groups. Intervention from week 35 of gestation until delivery and for 6 months within infants</td>
<td>1223 pregnant women 925 infants at risk for allergy</td>
<td>5.7x10^9 cfu (LGG) 5x10^9 cfu LC705 2x10^8 cfu BB99 2x10^8 (PJS)</td>
<td>Lactobacillus rhamnosus GG (ATCC53103) L. rhamnosus LC705 (DSM 7061) Bifidobacterium breve BB99 (DSM13692) Propionibacterium freudenreichii sp. Shermani JS (DSM 7076)</td>
<td>Probiotic treatment tended to reduce IgE-associated (atopic) diseases Respiratory infection incidence in the first two years of life was lower after synbiotic treatment</td>
</tr>
<tr>
<td>De Preter et al., 2008</td>
<td>Randomized, crossover intervention study for 4 weeks</td>
<td>53 healthy volunteers (25 women and 28 men; 19–26 years)</td>
<td>2x10 g lactulose + 2x250 mg placebo SB 2x15 g lactulose + 4x250 mg placebo SB 2x10^9 BB + 2x10 g placebo OF-IN 2x6.5x10^8 LeS + 2x10 g placebo OF-IN</td>
<td>Lactulose Oligofructose-enriched inulin (OF-IN) Lactobacillus casei Shirota (LcS) Bifidobacterium breve (BB) Saccharomyces boulardii (SB)</td>
<td>Lactulose, OF-IN, L. casei shirota or B. breve decreased beta-glucuronidase activity</td>
</tr>
</tbody>
</table>

GOS: Galacto-oligosaccharides; FOS: fructo-oligosaccharides; OS: Oligosaccharides; cfu: colony forming units; d: day.
developing gut wall, have also been suggested by Westerbeek et al.31 after administration of the combination of neutral oligosaccharides with acidic oligosaccharides (maximal dose of 1.5 g/kg/day added to breast milk or preterm formula).

As aforementioned, a well-proven effect of prebiotics has been described in infants but children and adolescents have so far inspired few clinical studies testing the effects of prebiotics on immunity30 and further studies are needed in this direction.

Probiotics have been more deeply studied in infancy and childhood, particularly in regard to the prevention of allergic diseases and reinforcement of the gut defence, stimulating a low-grade inflammation by activating the innate immune system and further production of IL-10. Lactobacillus rhamnosus GG (LGG) has extensively been studied on the prevention and treatment of acute infantile diarrhoea, antibiotic associated diarrhoea and atopic dermatitis with very interesting results.1,4,13,14 Bifidobacteria (i.e. B. infantis and B. bifidum) in combination with different strains of Lactobacillus spp. have been documented to be useful in diarrhoea prevention and treatment1. Lactobacillus coryniformis CECT5711 and Lactobacillus gasseri CECT5714 have also shown beneficial effects on intestinal flora of healthy children.36 The inclusion of yoghurt containing probiotics (375 g/day) over 10 weeks in a group of adolescents with anorexia nervosa (AN), showed a positive immunomodulator effect [higher CD4/CD8 ratio and increased IFN-γ production by stimulated peripheral blood mononuclear cells (PBMCs)]27 suggesting the potential impact of probiotics on this malnourished population.

The synbiotic formed by L. rhamnosus LCR35 plus a specific prebiotic preparation containing lactose (that LCR35 is able to hydrolyse) and potato starch used in the fermentation broth and the probiotic alone composed of the same fermentation broth seem to be able to significantly improve the manifestations of atopic dermatitis in children aged 2 years and over.39 Moreover, the treatment of the intestinal infections among children with a synbiotic product (containing B. bifidum, B. longum, L. casei strains and fibre) reduced the duration of the diarrhoea syndrome and provided a complete recovery of the intestinal microbiota balance.39 A positive effect on intestinal flora and systemic immune response (counts and activity of lymphocytes) in children with short bowel syndrome has been pointed out after 1 year of synbiotic therapy including Bifidobacterium breve, Lactobacillus casei and GOS.40 Other authors have suggested that in ill children receiving antibiotics, synbiotics may confer additional benefits by increasing bifidobacteria levels.41

Regarding long-term safety in infants, some aspects remain unclear. While feeding synbiotics to newborn infants has been suggested to be safe and to increase resistance to respiratory infections during the first 2 years of life,42 the real evidence about their clinical benefits and safety of prenatal and postnatal probiotic treatments still remains unclear.43 Hence, further research seems to be needed in this direction.

### Prebiotic and probiotic immune protection in adults and elderly

The modulation of the intestinal microbiota by dietary fibre has been established to serve as a useful adjunct in the treatment of gastrointestinal and inflammatory disease in adults.44-47 Recent evidence even suggests that inhibition of inflammatory processes may be an important mediator in the association between dietary fibre consumption and cardiovascular diseases (CVD). In fact, cross-sectional and randomized crossover intervention trials have demonstrated an association between dietary fibre and clinical inflammation biomarkers, such as C-reactive protein (CRP).48-50

In experimental models, prebiotics such as inulin and oligofructose have been associated with reduced mucosal inflammation and may offer an opportunity to

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**Fig. 1.—Main effects of fibres, prebiotics and synbiotics on the immune system in different life-stages in humans.**
Fibres, probiotics and synbiotics.
Immunomodulatory effect

prevent inflammatory bowel disease and other mucosal inflammatory disorders. Other health effects of prebiotics (prevention of diarrhoea, modulation of the intestinal microbiota metabolism, cancer prevention, positive effects on lipid metabolism, stimulation of mineral adsorption) are indirect, i.e. mediated by the intestinal microbiota, and therefore less-well proven. On the other hand, recent studies have shown the potentially extensive impact of prebiotics on gut microbiota composition, stimulating directly or indirectly putative beneficial gut commensals other than lactic acid bacteria, opening exciting areas of research for the discovery of new probiotic strains and synbiotic combinations.

Probiotics have been suggested to be capable to modulate the metabolism of short chain fatty acids, amino acids and plasma lipoproteins, demonstrating the diversity of synbiotic co-metabolic connections between the gut microbiota and the host. The prevention and/or treatment of infectious and antibiotic-associated diarrhoea, allergic diseases, inflammatory bowel disorders and prevention of respiratory tract infections by probiotics, have been documented in adults.

Regular, long-term intake of various synbiotics has been shown to improve adult health by reducing the incidence and severity of respiratory diseases during the cold season, suggesting a synergistic effect of both probiotic and prebiotic ingredients. Synbiotics have also been suggested to alter the composition of the colonic microbiota, reduce inflammatory processes in the gut mucosa, and have the potential to induce disease remission in inflammatory bowel diseases. In surgical patients, evidence from the existing randomized, controlled studies has shown that some synbiotics are able to prevent bacterial infections. Regarding aging, prebiotics, probiotics and synbiotics also might improve gut microbiota and the inflammatory condition of the elderly.

Since the early immune development in infants and the markedly declining immune function (immunosenescence) in the elderly have extensively been studied, prebiotic fibres, probiotics and synbiotics may be targeted for these specific age groups. Although the development of synbiotics to improve prevention and/or treatment of immune-related diseases have emerged as a new strategy for nutritionists and other health professionals, further intervention studies are needed to prove any added benefits or health effects of this combination of ingredients and scientific verification will be critical to the success of this concept. Moreover, further studies to ascertain the mechanisms, the optimal dose/duration and the long-term safety for the intervention in different age groups are also needed.

References


