AAP Reports on Use of Probiotics and Prebiotics in Children

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In recent years there has been increased interest in adding probiotics and prebiotics to nutritional products to optimize intestinal microflora. However, as with antibiotics, the use of these supplements should be supported by evidence-based medicine. The American Academy of Pediatrics (AAP) recently reviewed the medical uses of probiotics and prebiotics to help guide physicians in counseling parents about the use of these products as dietary supplements added to foods for children, including infant formula.

Infants have sterile gastrointestinal tracts at birth, but bacterial colonization occurs rapidly. Gestational age, mode of delivery, and diet seem to have significant effects on this process. Dysregulation of the intestinal mucosal defense system early in life is believed to be a factor in many chronic conditions, such as atopic diseases (e.g., asthma, eczema, allergic rhinitis) and autoimmune diseases (e.g., multiple sclerosis, type 1 diabetes mellitus, chronic inflammatory bowel disease). Because of their influence on intestinal microflora colonization and immune function, an infant's early diet and intestinal microbial environment are thought to be pivotal factors in his or her overall health.

Probiotics

Probiotics are supplements containing organisms that change the microflora of the host. These organisms are typically *Lactobacillus*, *Bifidobacterium*, and *Streptococcus* species. They are able to predominate and prevail over potential pathogenic microorganisms in the human digestive tract, and are thought to produce metabolic byproducts that function as immune modulators.

As of December 2010, at least two infant formulas that contained probiotics were being sold in the United States. One contained *Bifidobacterium lactis*, and the other contained *Lactobacillus rhamnosus* GG (LGG). The addition of probiotics to powdered infant formula has not been proven harmful to healthy term infants. However, there is no evidence of clinical effectiveness, and the routine use of these formulas is not recommended. No studies have compared the health benefits of using these formulas versus breastfeeding.

Probiotics should not be given to children who are seriously or chronically ill until the safety of these products has been established. The optimal duration of probiotic supplementation is not known, nor is the optimal dosage or species. The long-term effects on intestinal microflora in children also are not known.

ACUTE INFECTIOUS DIARRHEA

The use of probiotics early in the course of diarrhea from acute viral gastroenteritis may reduce its duration by one day in otherwise healthy infants and young children. This benefit is strain-dependent; LGG is the most effective probiotic reported. However, the evidence does not support the routine use of probiotics to prevent infectious diarrhea unless there are special circumstances (e.g., in child care centers). The use of the new pentavalent rotavirus vaccine will likely be ▶

more effective than the use of probiotics in preventing the most common form of acute infectious diarrhea in infants.

ANTIBIOTIC-ASSOCIATED DIARRHEA

There is some evidence to support the use of probiotics to prevent antibiotic-associated diarrhea, but there is no evidence that it is effective for treatment. LGG, *B. lactis, Streptococcus thermophilus,* and *Saccharomyces boulardii* were the most common probiotics used in randomized controlled trials (RCTs). There have been no RCTs examining the effects of probiotic use in children with *Clostridium difficile* antibiotic-associated diarrhea.

ATOPIC DISEASES

The intestinal bacterial flora of children with atopic disease has been proven to have more *Clostridium* and fewer *Bifidobacterium* organisms than that of children without atopic disease. For this reason, it has been hypothesized that the administration of probiotics to infants at risk of atopic disease—particularly those who are formula fed—would be beneficial. There is some evidence supporting the prophylactic maternal use of probiotics during pregnancy and the continuation of therapy in the mother and infant during lactation, but further studies are needed. Probiotic use has not been proven effective in the treatment of eczema.

NECROTIZING ENTEROCOLITIS

Preterm infants often have delayed and aberrant acquisition of normal digestive microflora, possibly because of restricted enteral feedings and frequent administration of antibiotics. These factors are thought to contribute to an increased risk of necrotizing enterocolitis in preterm infants. There is some evidence to support the use of probiotics in very low-birth-weight infants (birth weight of 1,000 to 1,500 g [2 lb, 4 oz to 3 lb, 5 oz]). However, the amount and specific type of probiotic are difficult to determine.

CHRONIC INFLAMMATORY BOWEL DISEASE

It is estimated that up to 70 percent of children and adults with chronic inflammatory bowel disease (i.e., Crohn disease or chronic ulcerative colitis) routinely use complementary and alternative medicine, including probiotics, as adjunctive or replacement therapy for prescribed medications. Theoretically, probiotics may be beneficial in the treatment of these conditions. However, the long-term benefit of using probiotics to treat Crohn disease requires further study and is not recommended in children. The results of RCTs in which probiotics were used to treat chronic ulcerative colitis are encouraging, but require further confirmation.

OTHER CONDITIONS

The sustained or long-term benefit of using probiotics to treat disorders such as irritable bowel syndrome, constipation, and extraintestinal infections requires further study; currently, use is not recommended in children. There is some evidence that probiotics may be beneficial in treating children with *Helicobacter pylori* gastritis and infantile colic; however, further study is needed before recommendations can be made. Probiotics have not been proven beneficial in treating or preventing cancer. There are safety concerns with the use of probiotics in infants and children who are immunocompromised, chronically debilitated, or seriously ill and who have indwelling medical devices.

Prebiotics

Prebiotics are supplements containing a nondigestible ingredient—usually in the form of oligosaccharides—that selectively stimulates the favorable growth or activity of indigenous probiotic bacteria. Although prebiotics are indigestible, their presence in the digestive tract enhances the proliferation of probiotic bacteria in the colon, especially *Bifidobacterium* species.

Human milk contains substantial quantities of prebiotics and is preferred for infants up to six months of age. The addition of oligosaccharides as prebiotics to infant formula is not unreasonable, but lacks evidence showing clinical effectiveness. It is not known whether their use is cost-effective.

The use of prebiotics in preventing or treating diseases in children has not been tested extensively in RCTs, but the available evidence shows that there may be some long-term benefit for the prevention of atopic eczema and common infections in healthy infants. However, confirmatory studies, especially in children who are given formula that is not partially hydrolyzed, are needed before recommendations can be made. ■

Answers to This Issue's CME Quiz

Q1. B	**Q5.** D	**Q9.** A, B, C, D
Q2. A	**Q6.** B, D	**Q10.** B, C, D
Q3. B, D	**Q7.** D	
Q4. B	**Q8.** B	