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Can probiotics change the gut's microbiome?

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H. Cody Meissner, M.D., FAAP

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Editor's note:*This is the third of a three-part series on prebiotics, probiotics and dietary supplements. Read the first article at http://bit.ly/347g6Nm, and the second article at http://bit.ly/2FL5zxI.*

Microbes in the human body outnumber human cells by 10:1, and the majority of microbes live in the intestine. The sum of the number of genes in all microbes in a person's microbiome is about 1,000 times the number of genes in the human genome.

Increasing evidence suggests that changes in a person's microbiome correlate with certain disease states. These observations have led to the theoretical possibility that manipulation of the microbiome might be a treatment option for certain diseases.

The extent by which probiotics modulate the host intestinal microbiota in a healthy individual is not clear. Theoretically, probiotics provide an opportunity to replenish the microflora following perturbation such as during antibiotic administration. In view of the highly diverse nature of the microbiome of the intestine and the large number of bacteria present in the intestine, it is difficult to evaluate minimal or partial distortion of the customary bacterial population that may occur during a disease state. In addition, the microbiome and the effect of antibiotics on the microbiome may differ from person to person.

A probiotic is intended to be alive when ingested, but the organism may not survive transit through the gut. To remain alive in the upper gastrointestinal tract, a probiotic requires the ability to survive the stomach's acidic environment and the ability to resist bile salt-mediated growth inhibition. Some probiotics resist bile degradation by secreting bile salt hydrolases that deconjugate bile acids. However, deconjugation of bile acids may impair digestion of essential dietary lipids.

Some people hypothesize that health benefits may be derived even from dead microbes. But to date, a consistent change in the gut's microflora has been difficult to determine in a disease state. Even if a microbiome change is identified in association with a disease state, it is difficult to define causality.

While the concept of altering the gut microflora may be reasonable intuitively, certain questions deserve consideration. Do orally administered microorganisms actually colonize the host mucosal surfaces? If so, for how long? Is colonization necessary to derive benefit? Most claims of gut colonization are based on recovery of excreted probiotic species in stool without evidence of mucosal colonization.

Attempts to document direct mucosal colonization by administered probiotics with sampling by endoscopy have yielded variable results. Some studies have shown colonization can occur, while others have shown limited if any colonization by the administered microbes. Few studies with follow-up beyond two weeks have

been performed. Available results suggest high variability among subjects as well as by strain contained in the probiotic.

Which of the following statements are true?

a) The microbiome of the gut includes the genetic material of all the microbes, including bacteria, fungi, protozoa and viruses that live in the intestinal tract.

b) A synbiotic refers to a preparation that is a combination of probiotic and a prebiotic that selectively favors the probiotic.

c) Vaginal seeding of an infant delivered by cesarean section is a safe practice.

d) Probiotics and prebiotics can be found in biscuits, cereals, chocolates and dairy products.

Answer: a, b and d are true

Safety of probiotics

Despite the absence of proven benefit, probiotics generally are assumed to be safe in healthy adults. Use in neonates, young children and people without an intact immune system has been associated with an increased risk of infection and other morbidities, especially among young infants, neonates with very low birth weight, neonates in the neonatal intensive care unit and immunocompromised patients.

Reported serious adverse events occurring as a complication of probiotic administration include bacteremia, fungemia, endocarditis, pneumonia and deep abdominal abscess. Reported mild adverse events occur infrequently and include rash, nausea, flatulence, abdominal bloating and constipation. Serious complications have occurred mostly in neonates and immunocompromised people. Complications appear to be less common in healthy individuals.

Rates of adverse events arising from use of prebiotics or probiotics are poorly understood, particularly when these products are administered to treat disease or to patients at increased risk of complications such as preterm infants. Most reports of complications are published as case reports, so overall adverse events rates are incompletely understood.

A recent systematic review of more than 300 probiotic trials noted that adverse events and safety concerns may be poorly reported, particularly in industry-sponsored trials (Bafeta A, et al. *Ann Intern Med.* 2018;169:240-247). The authors conclude “most studies of synbiotics, probiotics or prebiotics lack key safety parameters raising doubts about the confidence we can have in conclusions about the safety of these interventions.”

Neither the Food and Drug Administration nor the European Food Safety Authority has approved any probiotic for treatment or prevention of disease.

*Dr. Meissner is professor of pediatrics at Floating Hospital for Children, Tufts Medical Center. He also is an ex officio member of the AAP Committee on Infectious Diseases and associate editor of the AAP*Visual Red Book.

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