Probiotics:
A review for NPs

Abstract: While use of probiotics has increased, understanding when and how to use them can be confusing for patients. Nurse practitioners need to know the basics about the products, including which are evidence-based and most likely to provide a beneficial effect for a specific condition.

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A fter Mrs. S, a 70-year-old woman with intermittent bouts of diarrhea, watched a TV commercial touting probiotics, she wondered whether they would relieve her problem. Looking over the many brands and types on the pharmacy shelf left her confused. She made a mental note to ask about probiotics during her visit with the nurse practitioner (NP) the following week.

As primary care providers, NPs experience similar consternation regarding these over-the-counter (OTC) items, which, depending on the specific product’s intended use, can be FDA-regulated as dietary supplements, food ingredients, or drugs. To correctly advise their patients, NPs need basic information that will help them choose appropriate, quality products that will benefit patient health.

■ What are probiotics?
The word probiotics means “for life.” According to the World Health Organization’s consensus opinion, probiotics are live microorganisms, which, when administered in adequate amounts, confer a health benefit to the host. Often referred to as “good bacteria,” most probiotics are bacteria similar to the beneficial microbes naturally found in the human gut; these are used to target the microbes to promote health.

Keywords: probiotics; probiotic strains, health effects
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Although the timing of their origin is unclear, it is believed that probiotics colonize an infant’s gut at or soon after birth where they establish a barrier function for the normal microflora, thereby conferring immunity against some diseases. Probiotics also suppress pathogenic bacteria, modulate the immune system, and help fight disease through the suppression of intestinal proinflammatory cytokines, such as tumor necrosis factor.4

Probiotic confusion
Probiotics may be a source of confusion for the average consumer. Probiotics are readily available OTC and can be purchased in capsule, tablet, powder forms, or in yogurt—advertisers promote the advantages of probiotics without full explanation of the product. Little is said in regards to who might benefit or what precautions should be taken. NPs versed in the basics should educate their patients about probiotics, including the benefits, who should take them, the appropriate dose, and potential adverse reactions that may occur.

Main types
In the United States, the commonly used probiotics include Lactobacillus and Bifidobacterium, which include many specific types of bacteria within each of these two broad groups or genera (see Common strains of lactobacilli and bifidobacteria). As microorganisms, probiotics are classified by genus and species and identified at the strain level (for example, the genus Lactobacillus, species acidophilus, incorporates the strain designation ATCC 4356). Knowing this is important for prescriptive advice, as health benefits of probiotics may be strain-specific, and benefits of one type may not hold true for others.5

Who can benefit?
Probiotics use has increased. Often proposed for use to prevent respiratory/urinary tract infections and bacterial vaginosis, most research has been conducted regarding prevention and treatment of gastrointestinal problems. According to a survey of U.S. physicians (86% of whom were gastroenterologists), 93% of respondents reported that at least some of their patients use probiotics most commonly for irritable bowel syndrome (IBS), antibiotic-associated diarrhea (AAD), Clostridium difficile (C. difficile) colitis, pouchitis, and ulcerative colitis.3

Although health effects have been associated with probiotics, the evidence regarding whom it helps varies and is categorized into three levels (A through C) of recommendations for use. Once NPs check for indications of use and possible interactions with other medications, they can safely recommend probiotics that have strong evidence. (See Levels of evidence.)

Table: Common strains of lactobacilli and bifidobacteria

<table>
<thead>
<tr>
<th>Genera</th>
<th>Strains commonly used as probiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactobacillus (L)</td>
<td>L. acidophilus (LA-5 and NCFM), L. casei (DN-114 001, CRL 431, Lbc880r, shiratai), L. reuteri (RC-14, ATTC 55730), L. johnsonii (La1), L. plantarum (299V), L. rhamnosus (GG, GR-1)</td>
</tr>
<tr>
<td>Bifidobacterium (B)</td>
<td>B. animalis (lactisBb-12, DN 173 010), B. creve Yakult, B. infantis 35624, B. lactis HN019, B. longum (BBS36)</td>
</tr>
</tbody>
</table>

Levels of evidence

- **Level A** recommendation of use is based on strong, positive, well-conducted, controlled studies.
- **Level B** recommendation is based on positive controlled studies but in the presence of some negative studies.
- **Level C** recommendation is based on some positive studies but clearly an inadequate amount of data to establish the certainty of the Level A or Level B recommendations.


For children with rotaviruses, Level A evidence has been established using Lactobacillus rhamnosus GG (LGG) and Bifidobacterium lactis Bb-12 mainly for prevention of acute diarrhea as well as for atopic eczema related to cow’s milk allergy (see Recommendations for probiotic use for diarrhea).6

For adults with inflammatory bowel disease (IBD), Level A evidence has been shown with a combination of multiple probiotics, mainly VSL#3, which constitutes eight different strains, including three different strains of Bifidobacterium, four strains of Lactobacillus, and one strain of Streptococcus. (See Recommendations for probiotic use for IBD).6

In adults with IBS, evidence supports the use of Bifidobacterium infantis VSL#3 to help reduce the risk of persistent symptoms, and data are suggestive for beneficial effects in children with IBS as well.6,7

For adults in need of immune system enhancement or have AAD, probiotics are believed to build up the intestine’s
immunologic barrier, particularly through intestinal immunoglobulin A responses and the exclusion of intestinal inflammatory responses, which promote gut stabilization.6,7 Level A evidence for use of probiotics for immune enhancement has been shown with LGG, Lactobacillus acidophilus LA-5 and NCFM, Lactobacillus plantarum 299V, Bifidobacterium lactis HN019, and Lactobacillus johnsonii La1.6

### Precautions, risks, and benefits

The rapid growth in marketing and consumer interest and use have outpaced scientific research on the safety and efficacy of probiotics for specific health applications.8 While the Agency for Healthcare Research and Quality assessed the safety of probiotics and concluded that current evidence does not suggest a widespread risk of negative adverse reactions associated with their use, the data on safety—particularly long-term—are limited.9 It appears that most people do not experience harmful adverse reactions or have only mild gastrointestinal gas, but case reports of serious adverse reactions have necessitated ongoing research.

For example, LGG has been widely studied in clinical trials for a variety of conditions and generally found to be safe, receiving a level A recommendation; however, the long-term, cumulative effects of Lactobacillus and Bifidobacterium—especially in children—are unknown.6 Probiotics are not recommended for use in critically ill patients; the risk of serious adverse reactions may be greater in individuals who have underlying health conditions or for those who are immunocompromised or have cancer since parameters for safe administration are lacking.10

The quality of probiotics as well as the contents of some probiotic products have caused some concern. Some products have been found to contain smaller numbers of live microorganisms than expected. In addition, some products have been found to contain bacterial strains other than those listed as ingredients.11 Although manufacturers are not required to register their products with or get approval from the FDA before producing or selling dietary supplements, they are responsible for making sure that the products are safe, that the product label information is true and not misleading, and for reporting any serious adverse events associated with their use in the United States. All domestic and foreign companies that manufacture, package, label, or hold dietary supplements, including those involved with testing, quality control, and dietary supplement distribution in the United States, must comply with the Dietary Supplement Current Good Manufacturing Practices for quality control. The FDA is responsible for taking action against any unsafe product after it reaches the market.12

### Dose

The dose of probiotics used in clinical practice should be based on human studies that support the intended health benefit.6 Dosing is calculated in colony-forming units (CFUs), which indicate the number of viable microorganisms able to form a colony on an agar plate (for ex-
ample, one billion CFUs/gram). Taking "more" CFUs is not "better," and there is no "general dose." Rather, doses of probiotics vary depending on the strain recommended. Once the appropriate probiotic is advised, patients should follow the manufacturer's recommended dose found on the label.

### Advising Mrs. S

To determine whether Mrs. S would benefit from probiotics, the NP obtains a detailed history of her diarrhea and associated gastric discomfort, whether she has had periods of diarrhea and constipation without any acute changes in bowel habits, bleeding per rectum, fever, or any other alarm signals that would require a referral for a gastrointestinal workup. Once ascertained that Mrs. S's problem is simple diarrhea related to IBS, she could be advised to take either *Bifidobacterium infantis* 35624, one billion CFUs, according to the manufacturer's directions and cautions her about possible bloating and flatulence that might result.

### Patient education

A key feature of education concerning probiotics is that patients should refer to and follow the manufacturer's instructions on dosing, usage, and adverse reactions. (See Common brands with probiotic strains included.) Patients should be instructed to use the package insert to guide their use of probiotics and to consult with their NP should they have any questions. The following list of questions can be used as a tool to help guide NPs in their dialogue with patients as they recommend the appropriate probiotic:

- **Suitable:** Is the probiotic under consideration recommended with studies that fit the problem presented and follow the levels of recommendation for probiotics?
- **Precautions:** Does the patient have any contraindication that is listed for a particular probiotic? For example, immunocompromised patients should not take live probiotics.
- **Adverse reactions:** What are the associated adverse reactions? Does the use of a particular probiotic outweigh the risks of the adverse reaction profile? For example, flatulence is the most common adverse reaction associated with probiotics. Patients having severe diarrhea benefit from trading the diarrhea for flatulence, but patients with less severe diarrhea may not.
- **Affordable:** Can patients afford to pay for the probiotic that is being considered? Probiotics are an out-of-pocket expense generally not covered by insurance plans.
- **User-friendly:** Is the probiotic user-friendly for the individual patient’s lifestyle? For example, a probiotic that requires refrigeration will not work for a patient who travels or works away from home.

### NPs lead the way

Probiotics, substances that stimulate the growth of microorganisms (especially those with beneficial properties, such as those in the intestinal flora) are readily available in pill, capsule, powder forms, and food, such as yogurt. Consumers can easily be confused regarding what kind to take and for which purpose as well as the proper dose and possible adverse reactions. NPs must be versed in the basics and follow the evidence to provide correct, detailed, and current evidence-based recommendations. The dose of probiotics used in clinical practice should be based on human studies that support the intended health benefit.

#### Common brands with probiotic strains included

<table>
<thead>
<tr>
<th>Brand name*</th>
<th>Probiotic strain(s) included</th>
</tr>
</thead>
<tbody>
<tr>
<td>VSL#3</td>
<td><em>Bifidobacterium</em> (B) <em>breve</em>, <em>B. longum</em>, <em>B. infantis</em>, <em>Lactobacillus</em> (L) <em>acidophilus</em>, <em>L. plantarum</em>, <em>L. paracasei</em>, <em>L. bulgaricus</em>, <em>Streptococcus</em> (S) <em>thermophilus</em></td>
</tr>
<tr>
<td>Align</td>
<td><em>B. infantis</em></td>
</tr>
<tr>
<td>Culturelle</td>
<td><em>L. rhamnosus</em> GG</td>
</tr>
<tr>
<td>DanActive</td>
<td><em>L. casei</em></td>
</tr>
<tr>
<td>Mutaflor</td>
<td><em>E. coli</em> <em>Nissle</em></td>
</tr>
<tr>
<td>Florastor</td>
<td><em>Saccharomyces boulardii</em></td>
</tr>
<tr>
<td>GNC-probiotic complex 1.5</td>
<td><em>L. acidophilus</em>, <em>L. plantarum</em>, <em>L. rhamnosus</em>, <em>L. lactis</em>, <em>B. bifidum</em>, <em>L. salarius</em>, <em>S. thermophilus</em></td>
</tr>
<tr>
<td>Phillips’ Colon Health</td>
<td><em>L. gasseri</em> (previously identified as <em>L. acidophilus</em>), KS-13, <em>B. bifidum</em>, <em>B. longum</em></td>
</tr>
</tbody>
</table>

*Table developed by the authors based on information in the manufacturers’ labels. (NPs should read the complete manufacturers’ labels for information regarding strains and advise patients about usage based on the levels of recommendations for each specific probiotic.)*
patient-specific advice regarding usage. As part of their dialogue with patients, NPs should take into consideration the suitability of probiotics for each patient; any possible precautions or adverse effects; whether the patient can afford it; and whether probiotics can easily fit into the patient’s lifestyle.

REFERENCES

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