Metchnikoff earned the Nobel Prize in physiology for his research on immunity. He developed a theory of phagocytosis, a process performed by specialized cells to remove foreign bodies and thus fight infection, and promoted consumption of lactic acid bacteria, a microbe in sour milk.

Today’s products with live active bacteria cultures are based on Metchnikoff’s theory. Called probiotics, they have become a popular commodity and are used to promote gastrointestinal health and immunity. However, nearly a century after Metchnikoff’s recommendations, there are still many questions about them. The purpose of this article is to address these questions and enable readers to make informed choices about probiotics.

What Are Probiotics?
Probiotics are “friendly” microorganisms that, when consumed in certain amounts, may confer health benefits. They are listed by: (1) Genus, (2) Species and (3) Strain. For example, *Bifidobacterium infantis* 35624 is (1) Genus: *Bifidobacterium*, or B., (2) Species: *infantis* and (3) Strain: 35624.

On the other hand, pathogenic—unfriendly—microbes can cause disease within and beyond the gastrointestinal tract. Metchnikoff explained this concept with flair: “…Bacteria set up business in your interior departments; overwhelm friendly bacteria, called phagocytes, if you chance to be a little run-down; start gnawing around where they have no right to be; and the first thing you know, you are coming down with stomach trouble.”

In theory, by ingesting probiotics, we may be able to influence the integrity of the gut (a significant part of the immune system) and affect the course of health and disease.

Nevertheless, there is still more to learn, and the exact mechanisms by which probiotics reduce disease risk are not entirely clear.

How Do Probiotics Work?
Researchers believe that probiotics use their weaponry (such as natural toxins, fatty acids, hydrogen peroxide, antimicrobial agents, etc.) to create a less hospitable home for pathogens. In certain diseases associated with intestinal permeability (leaky gut), probiotics may serve as a barricade by wedging themselves between other cells and fortifying the gut’s mucosal barrier. In high numbers, they may crowd out or displace pathogens, the unfriendly germs.

Our gut contains hundreds of species of microbes and the composition is fairly stable. However, certain infections, autoimmune states, surgical procedures or drugs (e.g., antacids, antibiotics, chemotherapy) can alter the gut flora. During these vulnerable periods, germs that reside in the hospital, home, countryside, etc. can take up residence in gut flora and affect health in positive or negative ways.

When the constitution of the gut flora becomes irregular, an individual is more susceptible to diarrheal, inflammatory, and allergic diseases. The same thing is true for newborns. Because their gut is germ-free, any bacteria—good or
bad—can stumble on vacant terrain and build a colony. So, the aim of probiotic exposure (or colostrum and breast milk, in the case of infants) is to acquire helpful, or nonpathogenic, bacteria that restore the gut and support health.

What Conditions Might be Improved by Probiotics?
Probiotics have potential to minimize gastrointestinal conditions such as diarrhea, irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD), and they may improve health beyond the intestinal milieu. Probiotics also work indirectly to help recovery by enhancing compliance to therapy regimens. In one study, for example, children who were treated for Helicobacter pylori (peptic ulcer bacteria) with an antibiotic cocktail and probiotic (L. reuteri) had less intestinal distress. As a result, they were more likely to finish their course of treatment than those who used antibiotics alone.

Diarrhea
Antibiotic- and radiation-associated diarrhea is all too familiar for those who live with a weak immune system. A few studies have named probiotics that might minimize this problem: yeast Saccharomyces boulardii (Sb), L. rhamnosus (strain GG 53103 [LGG]), probiotic mixture VSL#3®, among others.
In addition, there is solid evidence for the use of LGG in the prevention and treatment of rotavirus-associated diarrhea. LGG shortens the duration of rotaviral diarrhea in children, but it does not help all forms of diarrhea. For example, there are still unanswered questions about the specific types of probiotic bacteria that are most effective for treating the different forms of diarrhea such as Clostridium difficile diarrhea. Just as specific brands of antibiotics work for certain types of infections, specific strains of probiotics work for certain types of diarrheal maladies.

Infectious and Inflammatory Bowel Disease
C. difficile-associated disease (CDAD) is a recurrent C. difficile-induced infection that is now a problem in the hospital and home. Repeated infections contribute to significant diarrhea and injury to the gut (e.g., pseudomembrane colitis). The buildup of C. difficile toxin is extremely dangerous in those with slow gut motility and immune dysfunction. In CDAD, the yeast Sb inhibits C. difficile toxin A-associated enteritis and may protect against intestinal inflammation. In addition, there are reports that certain probiotic mixtures such as VSL#3® may be useful for managing CDAD, bacterial overgrowth, post-operative pouchitis and IBD.

Irritable Bowel Syndrome
IBS has been associated with decreased nonpathogenic (“friendly”) colonies and increased Clostridium species. In clinical trials, certain probiotic strains (such as Bifidobacterium infantis, 35624), have shown promise in treating IBS when used with gut-directed antibiotics.

Future Areas
Other promising areas of strain-specific probiotic research include asthma, atopic dermatitis, bowel dysmotility, colon cancer and others. Yet, considerable work is still needed to confirm the potential health benefits and develop standard guidelines for patient groups. Likewise, more studies are needed before routine use of probiotics can be recommended for the public or special groups. Even if probiotics are proven to be effective in treating pathogens, such as C. difficile, they will not be curative when one has a defective antibody response. In such cases, probiotics should be used judiciously and not as a substitute for antimicrobial drugs or IgG replacement therapy.

What Should the Consumer Know?
Do not interchange different strains. You cannot substitute different strains of the same species and assume that you will get the effect as described in the literature. LGG, for example, may enhance IgA against rotavirus but you will not see this effect with other strains of lactobacillus.
Do not assume that the probiotic has colonized the gut. Less powerful probiotics colonize the human digestive tract only temporarily. Once you stop taking the probiotic, the bacteria will generally leave the gut. The more powerful probiotics are more likely to take up residence in the gut, but they are not always safe. Lactobacillus strains, for example, are resistant to vancomycin (an antibiotic for certain bowel infections).
Do not rely on a health food salesperson for advice. When considering a probiotic, it is essential to review the literature and identify the strain and dose that was used in clinical trials (see “Quick Checklist”). Then, consult with your physician.
Do your homework. Strains are generally not listed on product labels. Contact the manufacturer to find out what compounds are in the product. If the manufacturer cannot answer questions on the “Quick Checklist,” avoid using the product. When the treating physician is not familiar with the probiotic, it becomes the patient’s responsibility to find out the risks and benefits.

Consumer Beware!
The cost associated with probiotic preparations varies wildly. The most expensive may not be the best or the most appropriate. Shop wisely—and check with your physician.
Quick Probiotic Checklist
Answer the following questions and then talk with your physician:
1. What is the genus, species and strain of the probiotic?
2. What are the health claims and alleged benefits?
3. What type of study was done? Was it Phase II (randomized, double blind, placebo-controlled (DBPC))? Was it Phase III (DBPC and compared to a standard therapy)?
4. Who was represented in the study? Human subjects? Age? Gender? Animals?
5. What dose or serving was used in the studies or clinical trials?
6. What form was used? Capsule? Powder? Food?
7. What adverse reactions have been reported? Drug- or nutrient-interactions?
8. What are the risks of using this probiotic?
9. How should it be taken? With or without food? Before or after medication?
10. Does it contain any stabilizers or fillers? Is there potential for a food allergy?
11. What are the manufacturing practices? How is quality controlled?
12. What are proper storage conditions?

Are Probiotics Safe?
Reports of adverse effects in generally healthy persons or full-term infants have been limited, and evidence supports the safety of certain probiotics. For example, strains of *Lactobacillus* have been given to premature infants who lack a developed immune system. No significant adverse effects were reported in these studies.

On the other hand, there have been cases of *Lactobacillus* species associated with endocarditis, liver abscess and pneumonia. There are documented cases of *Sb fungemia* (fungus in the bloodstream) in high-risk patients who used...

Interview with Gary Elmer, PhD,
Department of Medicinal Chemistry,

Schulman: How do probiotics affect mucosal immunity?
Elmer: The immune system is stimulated by the microbes in our intestinal tract. If you get an imbalance or in the case of infants at birth (their intestinal tract is sterile), you pick up microbial flora from the environment, which wakes the immune system. All of the subtleties of this interaction are not entirely clear. But it is clear that, if you take a probiotic, there may be some benefits by stimulating your immune system.

Schulman: How far along are we when you compare probiotics now to the antibiotic revolution?
Elmer: I think we are in the infancy as far as trying to assess what probiotics can and cannot do. Just in the last decade, there have been some excellent probiotics made available, based on research and subsequent clinical trials, but we still have a long way to go. Only in the last few years have we developed some understanding about what probiotics can do for inflammatory and allergic diseases.

Schulman: For years, we did not understand how antibiotics worked and it took years before safe and effective drugs were available. Are probiotics following a similar pattern?
Elmer: I don’t think that probiotics have the same level of power as antibiotics but we don’t know the full spectrum of what they can do. Down the road, with genetics and strain selection, we may come up with a lot better probiotics than what we have now.

Schulman: In addition to preventing diarrheal disease, are there other areas that merit a closer look at probiotics for disease prevention and treatment?
Elmer: There is reason to believe that probiotics will be able to prevent asthma and allergies in childhood, and subsequently in adulthood, but the potential for prevention is not yet clear. An infant is usually born with a sterile gut and they pick up microbes from their environment. In the distant past, an infant’s microbial environment was very diverse. There were usually many siblings in a house and sanitation was different than what it is today. We may be doing a disservice by not exposing babies to non-pathogenic [harmless] organisms. This is called the hygiene hypothesis. It is still controversial but probiotics might be working in that manner.

Schulman: Are there single strains of probiotics that you feel are useful for certain conditions or is the jury still out on this?
Elmer: No, the jury is not out. Some strains act like drugs. LGG [*Lactobacillus rhamnosus strain GG*] may be useful for antibiotic-associated diarrhea and allergies but it does not seem to work for IBD [inflammatory bowel disease]. Each disease is different and it is not surprising that not all probiotics work for all GI diseases.

Schulman: Who should consumers turn to for advice or what kind of things they can do to make good choices?
Elmer: This is really difficult. You have to do your own research or talk with a healthcare provider.
Schulman: Obviously, patients should involve their doctor but I have found that patients are not getting answers from their healthcare providers.

Elmer: Absolutely. They should also talk with their pharmacists. We train our pharmacists about probiotics and there is some information online in databases. Natural Medicines Comprehensive Database [http://naturaldatabase.com] is a good one.

Schulman: There have been some questions about how other countries maintain different standards of quality and purity than we do. How do you extrapolate from one study to another?

Elmer: Many of the probiotics available in other countries, especially in European and Asian countries, are not available here. It is quite a dilemma. Studies may use certain strains and the results look encouraging. Then, you find that the strain is simply not available in this country.

Schulman: For the consumer, do you have any recommendations for finding probiotics that are safe and effective or is it buyer beware at this point?

Elmer: It is not quite that bad. I advise consumers to find probiotics that have been shown to be effective in sound clinical trials for the condition they have, if that is possible. The best-studied probiotics right now are LGG, Sb [S. boulardii], and VSL#3®, which is particularly good for IBD. There is another good, well-studied probiotic, L. Reuteri.

Schulman: A further complication for some patients with immune concerns is they have related GI problems, surgical procedures and dependence on medications that alter the flora. It seems that they might benefit from probiotics. However, patients get mixed messages from clinicians—some recommend probiotics and others warn against it. So, for this population, what would you suggest?

Elmer: It’s absolutely a dilemma. A few cases of bacteremia or fungemia [blood infections] with probiotics have been [reported] in populations that are immune suppressed or debilitated. The risk of problems with probiotics is very small, but there is a finite risk. The consumer has to weigh the benefits and risks.

Summary

Although probiotics hold promise for improving health outcomes, there is more work to be done. Consult your physician and give careful consideration to probiotic supplements before using them. Some things to consider are: effectiveness, dosage, safety record, manufacturer practices and strain. Finding the right bacteria for the right patient, at the right dose and the right time is not as easy as drinking sour milk.

Editor’s note: Although there may be a useful role for probiotics in PIDD, no quality studies have been performed. Because some PIDD patients may be at risk from even the bacteria in probiotics, you should check with your physician regarding the utility of probiotics in your healthcare regimen.

References


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