

Phages

Improve Intestinal and Immune Health

People are surprised to learn that about **70%** of the human immune system resides in the gut (known as the **microbiome**).

The **immune system** relies on the presence of healthy *intestinal bacteria* to protect the body from illness.^{1,2}

Age, poor diet, medications, and stress can upset the delicate balance of good to bad bacteria.³

An *imbalanced* gut microbiome contributes to autoimmune disorders, metabolic syndrome, diabetes, chronic fatigue, nonalcoholic fatty liver disease, obesity, and more.⁴⁻¹²

Life Extension® readers understand the value of taking a quality **probiotic** to help balance the **microbiome** and strengthen the immune system.

Incorporating **bacteriophages** with a **probiotic** takes this intestinal health strategy a step further.

Bacteriophages *selectively* target specific, harmful bacteria while leaving beneficial microbes to flourish. This was pioneered in Europe before the advent of **antibiotics**.¹³⁻¹⁵

Bacteriophages are especially beneficial when used in conjunction with **probiotics** because they act like advanced troops to clear the way for **beneficial bacteria** to flourish.

Laboratory studies show that when **probiotics** and **phages** are used in combination, **beneficial bacteria** grow to **thousands of times** their baseline rate.^{16,17}

How Gut Bacteria Affects the Entire Body

The microbiome comprises the trillions of microorganisms that live in the human gut.¹⁸ Today we know that the microbiome plays a critical role in health and disease.

The increased consumption of processed carbohydrates, meats, fats, preservatives, and other additives can alter our microbiome.¹⁹⁻²¹ In addition, antibiotic overuse kills both healthy and bad bacteria.²²⁻²⁴ As a result, our gut microbiome becomes disrupted and imbalanced.

Over time, an **imbalance** in the ratio of good to bad bacteria can trigger the development of chronic diseases in multiple areas of the body—not just those associated with the gut.⁴⁻¹²

We also recognize that allergic disorders, asthma, and even obesity are related to an unhealthy population of intestinal bacteria.^{25,26}

Fortunately, you can do something about it. By shifting your gut microbiome toward a more balanced, healthy profile, you can induce a positive impact on your overall health and well-being.¹⁸

Boosting Probiotics with Phage Therapy

A unique treatment known as **phage** therapy uses **bacteriophages** to selectively *reduce* harmful bacteria, making way for beneficial probiotic organisms to flourish. Using probiotics along with bacteriophages can quickly and effectively rebalance the gut microbiome.²⁷

Bacteriophages are submicroscopic packages of DNA or RNA enclosed in a protein envelope, and each one is chosen for its ability to attach to a unique strain of *unwanted* bacteria in the intestines. In other words, they *selectively* target specific, harmful bacteria, while leaving beneficial microbes to flourish.

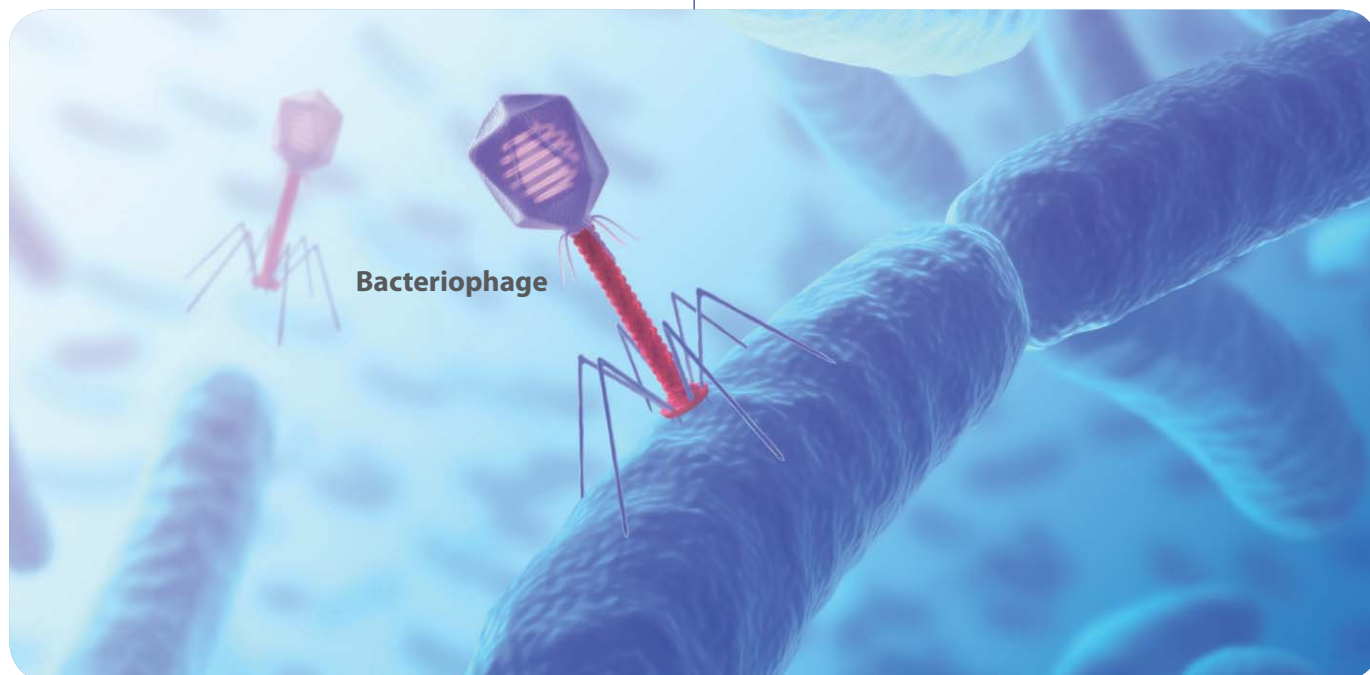
The Long History of Phage Therapy

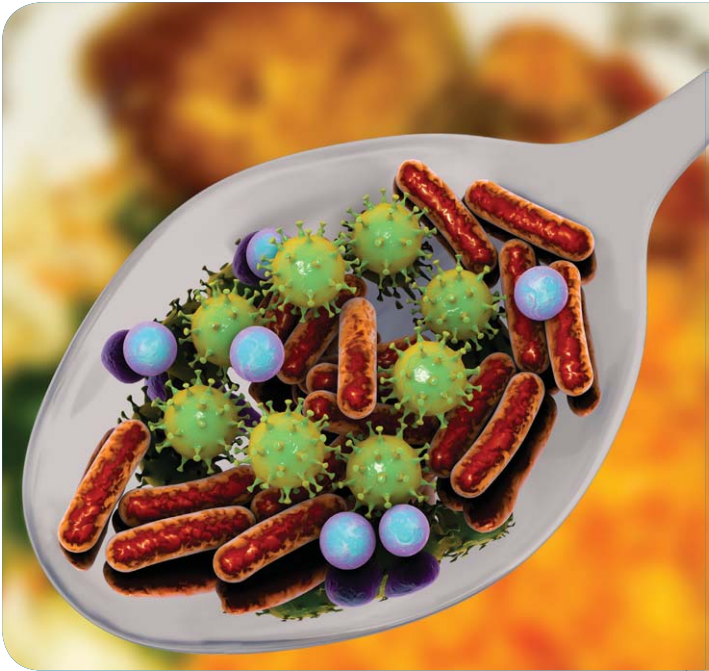
Using phages to control bacterial illnesses was pioneered in Eastern Europe before World War I.¹³⁻¹⁵

By the 1940s, industrial giants such as Eli Lilly and L'Oréal had developed bacteriophage “cocktails” for treating infections, but the advent of antibiotics quickly stole the spotlight (even though the effectiveness of **phages** was never in question).²²

We've come to recognize that one of the key drawbacks to antibiotics is that they employ a *mass-killing* technique that eliminates both detrimental and *healthy* bacteria, leaving us vulnerable to attack by other organisms.²⁸ In direct contrast to antibiotics, bacteriophages specifically eliminate only the detrimental bacteria while leaving healthy bacteria untouched.

Because of these targeted actions, the food industry now uses **bacteriophages** to control disease-causing organisms.²⁹⁻³¹ Many of these **phages** are classified by the FDA as **GRAS** (generally recognized as safe) and are commonly used for controlling bacteria ranging from *Listeria* in cheese and *E. coli* in meat, to *E. coli* on food-contact surfaces, to *Salmonella* in food.





What You Need to Know

Using Phage Therapy to Boost Probiotics

- Supplementation with potent **probiotics** is essential to supporting health throughout the body.
- Now, safe **bacteriophages** are available that *selectively* kill off undesirable bacteria, making room for beneficial bacteria to grow.
- Studies show that taking probiotics with *targeted* phages removes competing, unhealthy microbes to allow the beneficial probiotics to attain huge numbers.
- This approach can powerfully optimize digestive health and overall wellness by balancing the digestive tract microbiome.

A **phage cocktail** is effective within **hours**, not days, and in very small doses.¹⁶ As an added benefit, it functions not only in the large intestine, where bacterial imbalance (dysbiosis) is a problem, but also in the small intestine, where undesirable **bacterial overgrowth** can occur.

Animal studies have validated the benefits of using **probiotics** and **phage** therapy together. For example, when combined with a probiotic in an animal model, there was an exponential increase in beneficial bacteria with a parallel decrease in unfriendly flora such as *E. coli*.³²⁻³⁴

Let's examine more of the remarkable findings on this novel therapy.

Bacteriophage Potency

Scientists established the efficacy of bacteriophages in promoting healthy bacteria in a series of lab experiments.

In the first study, culture dishes were prepared with a beneficial bacterium (*Bifidobacterium longum*) along with competitive *E. coli* bacteria.

E. coli can be found in our gut, and although most strains are harmless, some can cause disease, and they can crowd out beneficial organisms.

Scientists in this study also prepared an identical set of dishes except for the addition of a **bacteriophage** mixture. After just five hours, the difference was striking.¹⁶

In the dishes without the **bacteriophages**, there was little growth of the desirable *B. longum* organism,

indicating their inability to compete with *E. coli*. But in the dishes containing the **bacteriophages**, colonies of *B. longum* skyrocketed to more than **7,000 times** their numbers compared to petri dishes without the bacteriophage. This was a clear demonstration of how the bacteriophage selectively targeted the *E. coli*, making room for the beneficial bacteria to multiply.¹⁶

In a similar study, the beneficial bacteria *Lactobacillus acidophilus* was grown along with *E. coli*. As expected, the *E. coli* greatly suppressed growth of the *L. acidophilus*.

But when the **phage** cocktail was added, *L. acidophilus* thrived, reaching colony counts that were **20-fold higher** compared to the culture not receiving the bacteriophages. Similar results were observed when beneficial *B. bifidum* bacteria were tested.¹⁶

Switching gears, scientists tested the capacity of the common prebiotic **inulin** to stimulate the growth of the beneficial *Lactobacillus paracasei*. Used alone, inulin failed to ensure the survival of the desired organisms. But using the combination of **inulin** plus the **phage** mixture produced an astonishing **nine million-fold** increase in the growth of the beneficial *L. paracasei*.¹⁶

These initial lab findings demonstrated the value of the **phage** mixture in promoting the growth and survival of beneficial organisms. Now it was time for scientists to test its potency in live subjects.

Phage Cocktail Validated in Gastrointestinal Environment

Researchers next demonstrated the effectiveness—and safety—of a **phage** cocktail when used in the gut of living lab rodents. One group of mice was given the probiotic *B. longum* along with the disease-causing *E. coli* strain H10407. The second group received the same mixture but with the addition of a **phage** cocktail specifically designed to target *E. coli*.¹⁷

After just 24 hours, the phage-treated group experienced a clear reduction in *E. coli* along with an impressive increase in beneficial *B. longum* bacteria.

The **phage** group showed the following effects on *E. coli*:

- **10-fold decrease** of *E. coli* in the small intestine;
- **100-fold decrease** of *E. coli* in the large intestine;
- **100-fold decrease** of *E. coli* in fecal matter.

The **phage** subjects showed the following approximate effects for *B. longum*:

- **100-fold increase** of *B. longum* in the small intestine;
- **100-fold increase** of *B. longum* in the large intestine;
- **40-fold increase** of *B. longum* in fecal matter.

The **phage-treated** group had improved digestive function and no detrimental changes, establishing overall safety and benefit.

By contrast, mice treated with only *E. coli* and *B. longum*—without the added **phage** cocktail—became constipated with intestinal segments showing swelling, redness, and leaks compared with healthy animals.

With so much scientific investigation into the multiple health benefits of a balanced microbiome, **phage therapy** is rapidly emerging as a new method of enhancing the benefits of **probiotics**.

Summary

Our gut **microbiome** greatly affects your immune system and overall health.

Probiotics have become popular to help balance intestinal flora.

Taking **bacteriophages** along with a **probiotic** *selectively* kills undesirable bacteria, making way for the good bacteria to survive and thrive.

When **probiotics** are accompanied by targeted **phage** therapy, beneficial bacteria multiply massively thanks to the removal of competing, unhealthy microbes.

Phage therapy shows promise in relieving the functional changes caused by gut microbiome imbalance. These may be especially valuable for aging individuals. ●

If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.



Proven Safety Record

Bacteriophages have been successfully used in numerous human clinical and therapeutic settings and have demonstrated an extremely strong safety profile.³⁵⁻³⁷ The reason for the very safe interaction between phages and human tissue likely results from human exposure to vast numbers of phages over the entire course of evolution. This naturally high human tolerance to bacteriophages contrasts sharply with the risks inherent in compounds that are relatively novel in human evolution—such as drugs.¹³

Superior Delivery System

Scientists have developed a powerful combination of **six** probiotic strains and **four** phages. But as beneficial as these six probiotics are, they have to be able to reach the intestines in order to work—and that requires remaining intact as they pass through the harsh, acidic environment in the stomach. This environment can limit the number of live microbes that reach their destination and, in turn, limit their beneficial effects.

A **dual-encapsulation** technology overcomes this problem by providing a **capsule-within-a-capsule**. The outer capsule contains the **phages**. The inner capsule contains the **probiotic** and remains intact longer to ensure that these bacteria reach the small intestine safely—delivering *unprecedented* numbers of live microbes to exactly where they are needed. This rebalances your microbiome to improve intestinal health and confers resistance to the bacterial imbalances that are associated with so many of the chronic degenerative diseases of aging.

References

- Furness JB, Kunze WA, Clerc N. Nutrient tasting and signaling mechanisms in the gut. II. The intestine as a sensory organ: neural, endocrine, and immune responses. *Am J Physiol*. 1999;277(5 Pt 1):G922-8.
- Bamola VD, Ghosh A, Kapardar RK, et al. Gut microbial diversity in health and disease: experience of healthy Indian subjects, and colon carcinoma and inflammatory bowel disease patients. *Microb Ecol Health Dis*. 2017;28(1):1322447.
- Biagi E, Franceschi C, Rampelli S, et al. Gut Microbiota and Extreme Longevity. *Current Biology*. 26(11):1480-5.
- Vyas U, Ranganathan N. Probiotics, prebiotics, and synbiotics: gut and beyond. *Gastroenterol Res Pract*. 2012;2012:872716.
- Cox LM, Blaser MJ. Pathways in microbe-induced obesity. *Cell Metab*. 2013;17(6):883-94.
- Everard A, Cani PD. Diabetes, obesity and gut microbiota. *Best Pract Res Clin Gastroenterol*. 2013;27(1):73-83.
- Knaapen M, Kootte RS, Zoetendal EG, et al. Obesity, non-alcoholic fatty liver disease, and atherothrombosis: a role for the intestinal microbiota? *Clin Microbiol Infect*. 2013;19(4):331-7.
- Ley RE. Obesity and the human microbiome. *Curr Opin Gastroenterol*. 2010;26(1):5-11.
- Sanz Y, Rastmanesh R, Agostoni C. Understanding the role of gut microbes and probiotics in obesity: how far are we? *Pharmacol Res*. 2013;69(1):144-55.
- Mortaz E, Adcock IM, Folkerts G, et al. Probiotics in the management of lung diseases. *Mediators Inflamm*. 2013;2013:751068.
- D'Aversa F, Tortora A, Ianiro G, et al. Gut microbiota and metabolic syndrome. *Intern Emerg Med*. 2013;8 Suppl 1:S11-5.
- Xu MQ, Cao HL, Wang WQ, et al. Fecal microbiota transplantation broadening its application beyond intestinal disorders. *World J Gastroenterol*. 2015;21(1):102-11.
- Abedon ST, Kuhl SJ, Blasdel BG, et al. Phage treatment of human infections. *Bacteriophage*. 2011;1(2):66-85.
- Bruynoghe R, and J. Maisin. Essais de thérapeutique au moyen du bacteriophage. *C. R. Soc. Biol.*. 1921;85:1120-1.
- Pelfrene E, Willebrand E, Cavaleiro Sanches A, et al. Bacteriophage therapy: a regulatory perspective. *Journal of Antimicrobial Chemotherapy*. 2016;71(8):2071-4.
- Supplier Internal Study. A Probiotic-Enhancing Prebiotic. Data on File. 2016.
- Supplier Internal Study. Bacteriophage Cocktail Mice Clinical Trials. Data on File. 2016.
- Khanna S, Tosh PK. A clinician's primer on the role of the microbiome in human health and disease. *Mayo Clin Proc*. 2014;89(1):107-14.
- Brown K, DeCoffe D, Molcan E, et al. Diet-induced dysbiosis of the intestinal microbiota and the effects on immunity and disease. *Nutrients*. 2012;4(8):1095-119.
- Pendyala S, Walker JM, Holt PR. A high-fat diet is associated with endotoxemia that originates from the gut. *Gastroenterology*. 2012;142(5):1100-1 e2.
- Van den Abbeele P, Verstraete W, El Aidy S, et al. Probiotics, faecal transplants and microbial network units to stimulate biodiversity of the human gut microbiome. *Microb Biotechnol*. 2013;6(4):335-40.
- Fortuna W, Miedzybrodzki R, Weber-Dabrowska B, et al. Bacteriophage therapy in children: facts and prospects. *Med Sci Monit*. 2008;14(8):RA126-32.
- Francino MP. Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances. *Front Microbiol*. 2015;6:1543.
- Watkins RR, Bonomo RA. Overview: Global and Local Impact of Antibiotic Resistance. *Infect Dis Clin North Am*. 2016;30(2):313-22.
- Rauch M, Lynch SV. The potential for probiotic manipulation of the gastrointestinal microbiome. *Curr Opin Biotechnol*. 2012;23(2):192-201.
- Ly NP, Litonjua A, Gold DR, et al. Gut microbiota, probiotics, and vitamin D: interrelated exposures influencing allergy, asthma, and obesity? *J Allergy Clin Immunol*. 2011;127(5):1087-94; quiz 95-6.
- Mimee M, Citorik RJ, Lu TK. Microbiome therapeutics - Advances and challenges. *Adv Drug Deliv Rev*. 2016;105(Pt A):44-54.
- Chan BK, Abedon ST, Loc-Carrillo C. Phage cocktails and the future of phage therapy. *Future Microbiol*. 2013;8(6):769-83.
- Garcia P, Martinez B, Obeso JM, et al. Bacteriophages and their application in food safety. *Lett Appl Microbiol*. 2008;47(6):479-85.
- Sillankorva SM, Oliveira H, Azeredo J. Bacteriophages and their role in food safety. *Int J Microbiol*. 2012;2012:863945.
- Woolston J, Parks AR, Abuladze T, et al. Bacteriophages lytic for Salmonella rapidly reduce Salmonella contamination on glass and stainless steel surfaces. *Bacteriophage*. 2013;3(3):e25697.
- Chibeu A, Lingohr EJ, Masson L, et al. Bacteriophages with the ability to degrade uropathogenic Escherichia coli biofilms. *Viruses*. 2012;4(4):471-87.
- Dalmasso M, de Haas E, Neve H, et al. Isolation of a Novel Phage with Activity against Streptococcus mutans Biofilms. *PLoS One*. 2015;10(9):e0138651.
- Kazmierczak Z, Gorski A, Dabrowska K. Facing antibiotic resistance: Staphylococcus aureus phages as a medical tool. *Viruses*. 2014;6(7):2551-70.
- Bruttin A, Brussow H. Human volunteers receiving Escherichia coli phage T4 orally: a safety test of phage therapy. *Antimicrob Agents Chemother*. 2005;49(7):2874-8.
- McCallin S, Alam Sarker S, Barretto C, et al. Safety analysis of a Russian phage cocktail: from metagenomic analysis to oral application in healthy human subjects. *Virology*. 2013;443(2):187-96.
- Sarker SA, McCallin S, Barretto C, et al. Oral T4-like phage cocktail application to healthy adult volunteers from Bangladesh. *Virology*. 2012;434(2):222-32.