

## News and Views

# The Role of Nutrition in Promoting Gut Health and Treating Chronic Illness Through the Attenuation of Inflammation

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## Abstract

### Description

Over the millennia, the human body and microorganisms such as bacteria, viruses, archaea, protozoa and parasites have coevolved together forming an intimate relationship. These microorganisms are found on the skin, in the mouth, genitourinary tract and most abundantly in the large intestine of the digestive tract. States of microbial dysbiosis contribute to chronic inflammation, which can lead to the pathogenesis and progression of numerous diseases. Micro- and macro-nutrients as well as dietary patterns like the Mediterranean diet can help improve health outcomes.

### Keywords

gastrointestinal microbiome; gastrointestinal tract/microbiology; probiotics; immune system phenomena/immunology; host-pathogen interactions; bacterial infections; metagenome; probiotics/therapeutic use; diet; dysbiosis; inflammatory bowel diseases

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## Introduction

The intestinal tract contains roughly a hundred trillion microorganisms, including more than 1,000 species and over 7,000 strains, collectively termed the gut microbiota.<sup>1</sup> Research has only just begun to realize the potential for gut health to promote overall health. The purpose of this brief review is to outline the integral relationship between the gut microbiota and the immune inflammatory response, as well as to highlight the viability of nutritional interventions to treat a host of chronic illnesses.

## Inflammation

The inflammatory response is paramount in maintaining innate immunity. Chemical messengers, called cytokines, play one role in this complex system. These signaling molecules are released primarily from macrophages and dendritic cells, but also from T-lymphocytes, natural killer cells, endothelial cells and mucosal epithelial cells. Once secreted, they bind to target cells and depending on the type, will either promote or attenuate inflammation.

With trillions of microorganisms, roughly 80% of the immune system resides in the human gut. The identification of specific bacterial species within the microbiota that may prevent or promote inflammation can elucidate the capacity for gut health to promote overall health. A number of individual strains have been shown to reduce inflammation. *Lactobacillus* and *Bifidobacterium* reduce inflammation by promoting anti-inflammatory cytokines; *Faecalibacterium prausnitzii*, *Lactobacillus reuteri*, *Lactobacillus fermentum* and *Bacteriodesokines thetaomicron* reduce pro-inflammatory cytokines.<sup>2-5</sup>

However, given the scope and complexity of the microbiota as a whole, individual microbes alone do not completely account for the true capacity of the microbiota to attenuate or promote inflammation. The complex relationships and the overall microenvironment of the microbiota are vital to host health. The bacteria in the microbiota are broadly categorized into

three groups: commensal bacteria, symbiotic bacteria and pathobiontic bacteria. Commensal bacteria do the host no harm but also do not offer direct benefit. Meanwhile, symbiotic bacteria offer direct benefit to the host (e.g., enzyme secretion and short chain fatty acid [SCFA] production). Lastly, pathobiontic bacteria confer harm to the host.<sup>6</sup> In this micro-environment, through competitive inhibition, the commensals, symbionts and pathobionts compete for nutrients and resources and prevent unchecked growth of any specific strains.<sup>7</sup> Inflammation ensues when either the pathobiontic bacteria increase or the commensal bacteria or symbiotic bacteria decrease. In this event, the relative abundance of pathobiontic bacteria becomes too great, which can create an inflammatory-rich environment by triggering pro-inflammatory cytokines.<sup>6</sup> Some factors that contribute to this imbalance include antibiotic usage<sup>8</sup> and poor diet.<sup>9</sup>

Potential pathologic sequelae of microbial dysbiosis and chronic inflammation include countless chronic illnesses. Increased levels of pro-inflammatory cytokines due to microbial dysbiosis have been observed amongst individuals with metabolic diseases, including obesity and hypertension;<sup>10</sup> renal diseases, like fatty liver;<sup>11</sup> as well as neurodegenerative diseases and psychopathologies, such as Parkinson's disease,<sup>12</sup> anxiety and depression.<sup>13</sup>

## Nutrients

Given such far-reaching implications, targeted use of specific nutrients and dietary patterns can attenuate inflammation by restoring gut health. Prebiotics are one such source of nutrition that can help treat chronic illnesses. Prebiotics are micronutrients that the human body is unable to utilize in energy metabolism and thereby promote a stable microbial environment by providing fuel for symbiotic bacteria. In doing so, symbiotic bacteria then produce a plethora of digestive enzymes as well as short chain fatty acids (SCFAs). SCFAs act as a fuel source for colonic enterocytes, as well as enhance coordination between tight junctions, thereby helping to maintain the integrity of the epithelial wall.<sup>14</sup> Absent of gut wall integrity, increased intestinal permeability allows pathobiontic bacterial endotoxins such as lipopolysaccharides (LPS) to activate inflammatory

cascades and has been associated with obesity and insulin resistance.<sup>14</sup> Furthermore, SCFAs help to regulate hepatic glucose, modulate appetite and aid in immune function.<sup>14</sup>

Increasing prebiotics in the diet is an effective method of reaping the benefits of SCFA production by gut microbes. Common sources of prebiotics include fiber and polyphenols. Fiber intake should reach at least 30 grams daily.<sup>9</sup> Food sources of fiber include legumes, whole grains and resistant starches, such as sweet potatoes and green bananas. Polyphenols, the phytonutrients responsible for giving fruits and vegetables their rich coloration can be found abundantly in foods and beverages, such as apples, apricots, bilberries, black currant, broccoli, red cabbage, white cabbage, cauliflower, fruit juices, black tea and red wine.<sup>15</sup> In sum, prebiotics provide the basis for a diverse and well-balanced microbial community by providing fuel to symbionts, which promote health through SCFA production.

However, research is beginning to shed light on the potential for probiotics to attenuate inflammation and treat chronic illnesses as well. Probiotics, literally meaning "for life," include microorganisms that, when administered in adequate doses, can benefit the host. Probiotics can be ingested in many forms including supplements; fermented foods like yoghurt, kimchi and kefir; as well as foods fortified with freeze-dried probiotics like breakfast cereals, breads, crackers, granola bars, chocolate and peanut butter.<sup>16</sup>

Some research suggests that *L. reuteri* can reduce cholesterol in those with hypercholesterolemia.<sup>17</sup> *S. thermophilus*, *L. bulgaricus*, *L. acidophilus* and *B. longum* seem to decrease small intestinal permeability, as well as improve mucosal barrier function.<sup>18</sup> *L. casei* and *B. bifidum* can improve body composition among obese individuals.<sup>19</sup> Additionally, a recent meta-analysis found moderate effect sizes across 105 studies for the use of probiotics in improving chronic inflammation, obesity, glucose control and fatty liver disease.<sup>20</sup> Although these data seem promising, specific prescriptions for the use of probiotics to treat such illnesses have yet to be laid out. Furthermore, as probiotics are considered dietary supplements in the United States and

are therefore not subject to FDA regulation or oversight, it is difficult to ensure the quality of the probiotic supplement regardless of form.<sup>21</sup> Future research should aim to establish dosing recommendations in order to serve the populations of individuals who are currently affected by chronic illnesses.

## Diet

Beyond the use of micronutrients, overall diet patterns can also be effective in improving gut health, reversing inflammation and treating chronic illnesses. The Mediterranean diet has been extensively studied and is lauded for its ability to reduce pro-inflammatory cytokines.<sup>22</sup> The Mediterranean diet is one rich in fruits, vegetables, whole grains, beans and nuts. Red meat is consumed sparingly; eggs, poultry and fish are consumed weekly. Olive oil is the primary cooking oil and red wine is consumed in moderation.<sup>23</sup> Not surprisingly, this diet is inherently high in prebiotics like polyphenols and fiber.

According to a recent meta-analysis by Ghosh et al.,<sup>24</sup> Mediterranean diet intake significantly altered the abundance of specific gut bacteria. Such changes were positively associated with greater physical well-being, cognitive function and anti-inflammatory cytokines; and were negatively associated with pro-inflammatory cytokines. The study concluded that Mediterranean diet adherence increases health-promoting bacteria and creates a stable microbial environment, which is associated with improved health outcomes, such as decreased inflammation.<sup>24</sup>

Unfortunately, the Mediterranean diet is, for the most part, the opposite of the standard American diet (SAD). While the Mediterranean diet is rich in complex carbohydrates (e.g., prebiotics) and monounsaturated fats, the SAD is laden with simple carbohydrates (e.g., sugar) and saturated fats. While the Mediterranean diet has been associated with numerous health benefits, the SAD has been associated with numerous health consequences. For example, highly refined starches and sugar have been shown to promote gut dysbiosis.<sup>9</sup> Furthermore, artificial sweeteners and emulsifiers that are found in many processed foods have also been shown to promote microbial dysbiosis.<sup>25,26</sup> Giv-

en the sensitivity of the microbiota to diet, and the consequences of dysbiosis, it is not surprising that the SAD is associated with higher rates of inflammation.<sup>27</sup>

In line with the Mediterranean diet, the FDA's My Plate, (formerly the food pyramid) recommends that half of any given plate include fruits and vegetables. The dietary recommendations also emphasize whole grains, and suggest that red meat be limited in favor of fish and poultry.<sup>28</sup> Taken together, diets resembling Mediterranean style diets, which are inherently high in prebiotics, can be an important consideration in treating a range of illnesses through the attenuation of gut-mediated inflammation.

## Summary

The vastly intricate and complex gut microbiota plays an important role in the promotion of human health. States of dysbiosis contribute to chronic systemic inflammation and ultimately, pathology. Fortunately, nutrition both in terms of micro- and macro-nutrient patterns serve as a viable strategy to address inflammation and treat chronic illnesses that currently affect such a significant portion of the population. Diabetes is the seventh leading cause of death in the United States; type 2 diabetes accounts for over 90% of all diagnosed cases of diabetes. According to the Centers for Disease Control and Prevention,<sup>1</sup> 30.3 million people in the U.S. have diabetes and an estimated 7.2 million are believed to be living with undiagnosed diabetes. At the same time, 84.1 million people are at increased risk for developing type 2 diabetes. Thus, more than 114 million Americans are at risk for developing the devastating complications of diabetes. The American Diabetes Association<sup>2</sup> estimated the total cost of diabetes in the United States in 2012 at \$245 billion, and the average medical expenditures for people with diagnosed diabetes at about \$13,700 per year. After adjusting for age group and sex, average medical expenditures among people with diagnosed diabetes were about 2.3 times higher than expenditures for people without diabetes.

## Conflicts of Interest

The author declares she has no conflicts of interest.

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### References

1. Cryan JF, Dinan TG. Mind-altering microorganisms: The impact of the gut microbiota on brain and behaviour. *Nature*. 2012;13:701-712. <https://doi.org/10.1038/nrn3346>
2. di Giacinto C, Marinaro M, Sanchez M, Strober W, Boirivant M. Probiotics ameliorate recurrent Th1-mediated murine colitis by inducing IL-10 and IL-10-dependent TGF-beta-bearing regulatory cells. *J Immunol*. 2005;174(6):3237-3246. <https://doi.org/10.4049/jimmunol.174.6.3237>
3. Sokol H, Pigneur B, Watterlot L, et al. Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc Natl Acad Sci U S A*. 2008;105(43):16731-16736. <https://doi.org/10.1073/pnas.0804812105>
4. Foligne B, Nutten S, Grangette C, et al. Correlation between in vitro and in vivo immunomodulatory properties of lactic acid bacteria. *World J Gastroenterol*. 2007;13(2):236-243. <https://doi.org/10.3748/wjg.v13.i2.236>
5. Round JL, Mazmanian SK. The gut microbiota shapes intestinal immune responses during health and disease [published correction appears in *Nat Rev Immunol*. 2009 Aug;9(8):600]. *Nat Rev Immunol*. 2009;9(5):313-323. <https://doi.org/10.1038/nri2515>
6. DeGruttola AK, Low D, Mizoguchi A, Mizoguchi E. Current understanding of dysbiosis in disease in human and animal models. *Inflamm Bowel Dis*. 2016;22(5):1137-1150. <https://doi.org/10.1097/MIB.0000000000000750>
7. Kamada N, Chen GY, Inohara N, Núñez G. Control of pathogens and pathobionts by the gut microbiota. *Nat Immunol*. 2013;14(7):685-690. <https://doi.org/10.1038/ni.2608>
8. Yoon MY, Yoon SS. Disruption of the gut ecosystem by antibiotics. *Yonsei Med J*. 2018;59(1):4-12. <https://doi.org/10.3349/ymj.2018.59.1.4>
9. Makki K, Deehan EC, Walter J, Bäckhed F. The Impact of Dietary Fiber on Gut Microbiota in Host Health and Disease. *Cell Host Microbe*. 2018;23(6):705-715. <https://doi.org/10.1016/j.chom.2018.05.012>
10. Boulangé CL, Neves AL, Chilloux J, Nicholson JK, Dumas ME. Impact of the gut microbiota on inflammation, obesity, and metabolic disease. *Genome Med*. 2016;8(1):42. Published 2016 Apr 20. <https://doi.org/10.1186/s13073-016-0303-2>
11. Quesada-Vázquez S, Aragonès G, del Bas JM, Escoté X. Diet, Gut Microbiota and Non-Alcoholic Fatty Liver Disease: Three Parts of the Same Axis. *Cells*. 2020;9(1):176. Published 2020 Jan 10. <https://doi.org/10.3390/cells9010176>
12. Campos-Acuña J, Elgueta D, Pacheco R. T-Cell-Driven Inflammation as a Mediator of the Gut-Brain Axis Involved in Parkinson's Disease. *Front Immunol*. 2019;10:239. Published 2019 Feb 15. <https://doi.org/10.3389/fimmu.2019.00239>
13. Peirce JM, Alviña K. The role of inflammation and the gut microbiome in depression and anxiety. *J Neurosci Res*. 2019;97(10):1223-1241. <https://doi.org/10.1002/jnr.24476>
14. Morrison DJ, Preston T. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. *Gut Microbes*. 2016;7(3):189-200. <https://doi.org/10.1080/19490976.2015.1134082>
15. Aherne SA, O'Brien NM. Dietary flavonols: chemistry, food content, and metabolism. *Nutrition*. 2002;18(1):75-81. Accessed October 12, 2018. [https://doi.org/10.1016/S0899-9007\(01\)00695-5](https://doi.org/10.1016/S0899-9007(01)00695-5)
16. Fenster K, Freeburg B, Hollard C, Wong C, Rønhave Laursen R, Ouwehand AC. The Production and Delivery of Probiotics: A Review of a Practical Approach. *Microorganisms*. 2019;7(3):83. Published 2019 Mar 17. <https://doi.org/10.3390/microorganisms7030083>
17. Jones ML, Martoni CJ, Prakash S. Cholesterol lowering and inhibition of sterol absorption by *Lactobacillus reuteri* NCIMB 30242: A randomized controlled trial. *Eur J Clin Nutr*. 2012;66(11):1234-1241. <https://doi.org/10.1038/ejcn.2012.126>
18. Zeng J, Li YQ, Zuo XL, Zhen YB, Yang J, Liu CH. Clinical trial: effect of active lactic acid bacteria on mucosal barrier function in patients with diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther*. 2008;28(8):994-1002. <https://doi.org/10.1111/j.1365-2036.2008.03818.x>
19. Colica C, Avolio E, Bollero P, et al. Evidence of a new psychobiotic formulation on body composition and anxiety. *Mediators Inflamm*. 2017;2017:5650627. <https://doi.org/10.1155/2017/5650627>
20. Koutnikova H, Genser B, Monteiro-Sepulveda M, et al. Impact of bacterial probiotics on obesity, diabetes and non-alcoholic fatty liver disease related variables: A systematic review and meta-analysis of randomised controlled trials. *BMJ*

- Open*. 2019;9(3):e017995. Published 2019 Mar 30. <https://doi.org/10.1136/bmjopen-2017-017995>
21. Quigley EMM. Prebiotics and Probiotics in Digestive Health. *Clin Gastroenterol Hepatol*. 2019;17(2):333–344. <https://doi.org/10.1016/j.cgh.2018.09.028>
  22. Schwingshackl L, Morze J, Hoffmann J G. Mediterranean diet and health status: Active ingredients and pharmacological mechanisms. *Br J Pharmacol*. 2020;177(6):1241–1257. <https://doi.org/10.1111/bph.14778>
  23. Thompson JL, Manore M, Vaughan LA. *The Science of Nutrition*. 4th edition. Boston: Pearson; 2017.
  24. Ghosh TS, Rampelli S, Jeffery IB, et al. Mediterranean diet intervention alters the gut microbiome in older people reducing frailty and improving health status: the NU-AGE 1-year dietary intervention across five European countries [published online ahead of print, 2020 Feb 17]. *Gut*. 2020;gutjnl-2019-319654. <https://doi.org/10.1136/gutjnl-2019-319654>
  25. Chassaing B, Koren O, Goodrich JK, et al. Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome [published correction appears in *Nature*. 2016 Aug 11;536(7615):238]. *Nature*. 2015;519(7541):92–96. <https://doi.org/10.1038/nature14232>
  26. Nettleton JE, Reimer RA, Shearer J. Reshaping the gut microbiota: Impact of low calorie sweeteners and the link to insulin resistance? *Physiol Behav*. 2016;164(Pt B):488–493. <https://doi.org/10.1016/j.physbeh.2016.04.029>
  27. Lassale C, Batty GD, Baghdadli A, et al. Healthy dietary indices and risk of depressive outcomes: A systematic review and meta-analysis of observational studies [published correction appears in *Mol Psychiatry*. 2018 Nov 21;]. *Mol Psychiatry*. 2019;24(7):965–986. <https://doi.org/10.1038/s41380-018-0237-8>
  28. ChooseMyPlate. <https://www.choosemyplate.gov/>. Accessed March 12, 2020.