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The Interaction between Dietary Components, Gut Microbiome, and Endurance Performance

Basista Rabina Sharma and Ravindra P. Veeranna

Abstract

Research so far indicates that gut microbiome and diet interactions influence obesity, diabetes, host immunity, and brain function. The ability of athletes to perform to optimum for a more extended time, as well as the ability to resist, withstand, recover from, and have immunity to fatigue, injury depends on the genetic factor, age, sex, training history, psychological factors, mode, intensity and frequency of training and their interactions with the external dietary components. However, recent evidence indicates that the gut microbiome may also potentially influence the development of endurance in response to the type and composition of the external diet, including several food supplements. Thus, the gut microbiome has become another target in the athlete's pursuit of optimal performance. This chapter discusses the effect of exercise on the gut microbiome, the interplay between dietary components and supplements on the gut microbiome, and its impact on endurance performance.

Keywords: Diet, Gut, Endurance

1. Introduction

Endurance exercises can be defined as prolonged exercises like running, cycling, cross-country skiing, aerobics and swimming, often involving resistance [1]. Endurance exercises require systemic and muscle-based physiological and biochemical responses to complete the endurance activity [2]. The athletes expose their bodies beyond their physiological circumstances, which affect the homeostasis, overwhelming normal tissue function [3]. Prolonged physical exercise will force body to defend against the events that will result in the synthesis of proteins, releasing of hormone, changes in body fluid as well as metabolic balance [4]. In order to adapt toward the endurance exercise, an individual should improve his mechanical, neuromuscular, metabolic and contractile functions in muscle, rebalance of electrolytes and decrease in glycogen storage [5]. Furthermore, endurance exercise will cause muscle damage, alterations in intestinal permeability, systematic inflammation, immune response and oxidative stress in the athletes [6]. Excessive exercise will effect the blood flow, resulting in loss of fluids and electrolytes. The body will start synthesizing glucocorticoids and adrenaline hormones to re-establish homeostasis [7].

Human gut microbiota act as an endocrine organ and plays a significant role in energy harvesting, nutrient uptake, vitamin synthesis, modulation of inflammatory, host immune response etc. Several intrinsic and extrinsic factor effect the gut microbiota, which will lead to dysbiosis. Some factors include diet, lifestyle,

environment, antibiotic use, age and birth delivery route. Recent findings reported that exercise induced changes in gut microbiota, through mechanisms not well-understood results modifications in metabolism, physiology, immunity and behavior in host [8]. Dysbiosis depends on the intensity, types and timing of excessive exercise [9]. Human gut microbiota also influences muscle mass and aging of the body. Studies reported the reduction of microflora in gut microbiota having anti-inflammatory and proanabolic effects [10]. To adapt to the excessive physical load and increased energy consumptions, individuals performing excessive exercise e.g. athletes, should balance gut microbiota composition, which can only be done by adopting good dietary habits and using sports nutritional supplements. Gut microbiota plays significant role in the wellbeing, health and sports performance in athletes [11]. This chapter, discusses the effect of exercise on the gut microbiome, the interplay between dietary components and supplements on the gut microbiome, and its impact on endurance performance.

2. Gut Microbiota

Gut microbiota refers to specific microbial population in the gut that includes the bacterial and viral origin and is considered as non-pathogenic [12]. Gut microbiota coordinately works with the immune system of the host, to protect from pathogen colonization and invasion. Gut microbiota act as a good source of essential nutrients and vitamins, also help in the extraction of nutrients, including vitamins and SCFA from food. In the end, host depends on its intestinal microbiota, and intestinal microbiota contribute to the host's health [13]. The interplay between gut microbiota and host physiology influences the metabolic phenotype, stress response of the host. Further, the equilibrium between the microbial diversity is essential maintain the host homeostasis including energy metabolism, oxidative stress, hydration status, immunity response, systematic inflammatory response and brain-gut axis [14]. The dysbiosis in the gut microbiota may contribute to the onset of chronic conditions including inflammatory and irritable bowel diseases, gastrointestinal symptoms linked to exercise, colorectal cancer, obesity, diabetes, metabolic syndrome, allergy, depression, anxiety [15]. The factors that influence host intestinal microbiota are genetic, lifestyle including physical activities, diet and environmental factor [9]. Physical activity is linked to specific markers of intestinal health [16–18]. Some of the evidence suggests that exercise positively influence the gut microbial community, which is beneficial to the host [19].

2.1 Effect of diet on gut microbiota

The human diet is very complex, where foods are not consumed separately, and nutrients are act synergistically. Hence, the dietary patterns are considered the key element of human health. Dietary habits includes the diet variety, nutrient adequacy, intake of healthy food, and considerable amount of less healthy foods [15, 20]. Changes in dietary habits leads to change in the GM. GM since diet has a significant role in determining the composition of GM [21, 22]. Alternative or mismanagement in dietary patterns may harm the population of healthy microorganisms in GM. Researchers have identified that prevailing dietary patterns in US, European and Asian populations, may have a risk of diabetes and obesity [23, 24]. *Bifidobacteria*, *Clostridium* and *Bacteroidetes* decreases due to low carbohydrate diet as carbohydrate is the source of energy for these microbes [25, 26] studies have found that intake of dietary fiber in the diet increases the short chain fatty acid (SCFA) producing bacteria in the GM. The western diet rich in animal protein and fat showed a significant

reduction in gut microbiota diversity due to the low amount of dietary fibers [27]. The mediterranean diet includes intake of various polyphenol rich fruits, herbs and vegetables which lower down the risk of metabolic diseases especially diabetes and obesity [28]. Intake of a high protein diet leads to increased *Bacteroidetes*, *Lactobacillus*, *Bifidobacteria* which will benefit the host for metabolism, immune system and nervous system [29]. Keto diet will lead to Dysmicrobism because microbiota need carbohydrates as a source of energy [30]. Intake of high-fat diet will result in impairments in colonic epithelial integrity and barrier function due to the decrease in *Bacteroidetes* and *Firmicutes* [31].

2.2 Effect of endurance performance on gut microbiota

The effect of excessive exercise on human gut microbiota compositions depends on several factors like body fat, age, diet, timing, training status of the particular subjects. Effect of exercise start early in life. Physical activities promote increases in *Bacteroidetes* and decreases in the *Firmicutes* phylum in the gut of young than in adults, also increases in lean body mass through the adaptation of host metabolism [32, 33]. Several have reported that microbial population altered by exercise favour the development of the brain [9]. Several pieces of evidence reveal the present of diverse microflora in an athlete, with an abundance of *Bacteroidetes*, *Akkermansia*, *Veillonellaceae*, *Prevotella*, and *Methanobrevibacter* [32]. A higher amount of *Prevotella* and *Methanobrevibacter smithii* were found in professional as compared to amateur cyclists. This microflora is known to involve in carbohydrate and energy metabolism in the human body [34, 35]. Overweight adults, following a fiber and whole-grain-rich diet for six weeks, the presence of *Prevotella* abundance predictive of weight loss, suggesting that enterotype should be considered in personalized nutritional strategies to counteract obesity [36, 37]. One of the studies shows the difference of microflora between active and sedentary Women. Active women have a higher amount of health-promoting bacterial species, including *Akkermansia muciniphila*, *Roseburia hominis*, *Faecalibacterium prausnitzii* and *Coprococcus* genus [38, 39]. *Akkermansia muciniphila* is a mucin degrading bacteria that protects the intestinal lumen, and its levels are, negatively associated with metabolic disorder in patients with inflammatory bowel diseases [40, 41]. In addition, exercise has shown positive impact on the gut mucus layer, which is an essential substrate for the mucosa-associated bacteria e.g. *Akkermansia muciniphila*, *Roseburia hominis* and *Faecalibacterium prausnitzii* were known to produce butyrate, showing a positive impact on intestinal function and metabolism of lipid, thereby having anti-inflammatory properties [42]. Other studies have also reported the abundance of *Coprococcus* genus in active women [32]. One of the study conducted between lean and obese adults performing endurance exercise under proper dietary control reveal the abundance of butyrate producing taxa in lean adults as compared to the obese adults [43]. Similar studies reported by Galle, (2019), showed the abundant of *Faecalibacterium* sp. in lean adults compared to obese adults [44]. This study confirmed the influence of BMI in gut microbiota. Thereby normalizing the BMI, age and diet can have a beneficial effect on individuals, by increasing butyrate producing taxa.

Recently, it was reported that *Veillonella* is a performance enhancing microbe known to utilize lactate and produce propionate [45]. Similar studies reported that lactate can be converted into propionate by the *Veillonella* [46]. Thus the production of SCFA by gut microbiota will promote health benefits toward the host during exercise, thereby contributing to exercise-induced adaptation. The SCFA produce by the microbiota fermentation will later act as an energy source for the liver and muscle cells, thereby improving endurance performance. Moreover, it is needed to balance the gut microbiota composition over time.

3. Dysbiosis of gut microbiota during endurance performance

The dysbiosis in the GM is linked to various pathophysiological conditions such as intestinal disorders (inflammatory bowel disease, coeliac disease, irritable bowel disease) and extra-intestinal disorders (allergy, metabolic syndrome, asthma, cardiovascular disease, obesity, oxidative stress) [47]. The beneficial bacteria play an essential role in controlling the fermentation and absorption of dietary nutrients such as SCFAs [48]. The dysbiosis in the microbiota influences the development of disease which involved the pivotal mutualistic relationship between colonic microbiota, their metabolic product and the host immune system. Recent evidence has implicated the influence of excessive exercise on GM dysbiosis [49]. Studies in mice found that excessive exercise negatively impacts immunity, substance and energy metabolism, and gut microbial diversity [50].

Generally, it is believed that exercise is beneficial for the gut, but athletes with regular training and exercise have been reported to experience gastrointestinal disorders termed exercise-induced gastrointestinal syndrome. The frequency of developing the syndrome depends on numerous factors like sport type, the intensity of exercise, gender and syndrome often observed: loose stool, diarrhea, abdominal pain, intestinal bleeding in the lower digestive tract [51, 52]. There are two pathways suggested as causative for this disorder: Circulatory- gastrointestinal pathway and neuroendocrine-gastrointestinal pathway. In Circulatory-gastrointestinal pathway, high intensity exercise cause gut ischemia-reperfusion, which is a factor associated with site specific oxidative stress intestinal injury and in Neuroendocrine-gastrointestinal pathway, both physical and psychological stresses alter the gut motility and transit through enteric nervous activity which causes gut malabsorption of nutrients [53–55]. Studies found that intense endurance running (triathletes) lead to malabsorption of carbohydrates [27]. Evidence suggests that female endurance runners had a higher abundance of inflammation related bacteria and a higher concentration of succinate in the intestinal lumen due to dysbiosis, thus affecting the endurance performance [56].

3.1 Energy metabolism

During endurance exercise, energy availability is the essential limiting factor, and restoring the cellular energy homeostasis is a must. There is a complex relationship between gut microbiota and host's energy metabolism. Gut microbiota increases the ability to harvest the energy from digested food, thereby producing metabolites and microbial products (SCFA, secondary bile acids, and lipopolysaccharides). These microbial products will later modulate appetite, energy uptake and storage, gut motility and energy expenditure [57]. Healthy gut microbiota can exert positive effects in athletes. One of the studies reported that physical exercise and associated dietary adaptation are linked with changes in the gut microbial diversity [58]. Supplementation of probiotic bacteria *Lactobacillus plantarum* TWK10 improves energy metabolism. It transports the host fatty acid to the organ via bloodstream, further metabolized in the mitochondria to generate energy [59].

3.2 Immune response

During endurance exercise, immune response activation plays an important role. Some evidence suggests that, prolonged periods of intense exercise suppress the immune response, including monocyte, granulocyte, leukocyte count, and serum immunoglobulin levels among individuals [60]. Intense exercise training

increased the number of pro-inflammatory cytokines, also anti-inflammatory modulator, intestinal lymphocytes. These will lead to the fluctuation of gut microbiota diversity and in their secreted metabolites, increase hyperthermia, gastrointestinal permeability, destruction of gut mucous membrane thickness and weakens the activity of antioxidant enzymes [61]. Studies found that strenuous exercise suppresses the lymphocytes proliferation, levels of secretory IgA in saliva and modulates the synthesis of inflammatory cytokines [62]. Studies suggest that monitoring the gut microbiota diversity and modulating it by the supplementation of probiotics and prebiotics will be more cost effective compared to the utilization of drugs [63].

3.3 Oxidative stress

During endurance exercise, oxygen consumption increases which will cause disturbance in intracellular pro-oxidant-antioxidant homeostasis [64]. Modulations of oxidative and nitrative stress can control tissue damage, bacterial translocation and intestinal permeability. Enzymatic and nonenzymatic antioxidant protect excessive oxidative damage, and therefore, consumption of antioxidant would be a beneficial to control the oxidative damage [65]. The relationship between gut microbiota and controlling GI redox is still not clear. Some data found that *Lactobacillus* and *Bifidobacterium* levels are negatively correlated with oxidative stress, while the *Escherichia coli* population is positively correlated with oxidative stress [66]. Study in mice, found that higher levels of *Bacteroidetes* protect against intestinal infection by suppressing pro-inflammatory and pro-oxidant responses [67].

3.4 Dehydration status

During endurance exercise, an increased in fluid loss from sweating will lead to dehydration [68]. One of the main functions of mucosal epithelial cells is transportation of electrolyte. For proper functioning and protection of intestinal barrier, proper water transport and mucosal hydration are necessary [69]. During excessive exercise, studies found that healthy gut microbiota can maintain proper hydration and will prevent inflammatory response. Evidence suggest that activation of Cl⁻ secretion alters the colonic inner mucus layer which lead to the increased in abundance of *Firmicutes* phylum and *Alistipes* genera [70]. In order to obtain a good hydration state and protect intestinal barrier in athletes, it became necessary to understand the role gut microbiota on water transport, diet and mucus intestinal layer.

4. Diet modulation of gut microbiota in athletes

Dietary changes are the most significant factor in altering gut microbiota both in infancy and in adulthood. Recently, it has been found that probiotics, polyphenols, prebiotics and antibiotics can modulate the gut microbiota community [71]. Many evidence have been reported, how probiotics, prebiotics alter the gut microbiota population which will benefit individuals suffering from metabolic disorder, gut permeability, inflammation, immune system and energy metabolism [14, 72].

Probiotics are food supplements that contained a live microorganism (Lactic acid bacteria), which confer a health benefits a health benefit for the host [73]. Many probiotics products are available in the markets like fermented milk and yogurt, etc. [74]. Consuming probiotics has a positive effect gut microbiota's population which will influences the immune function as well as intestinal epithelium

cell proliferation, function and protection in the athletes. Various double-blind clinical trials, cross-over pilot studies show that supplementation of probiotic bacteria can modulate the gut microbiota and have a beneficial effect on the individual with regular exercise training (listed in **Table 1**).

The effect of probiotic bacteria in athletes has been reported and assists athletes with respiratory and gastrointestinal disorders during the specific training periods. However, the effects of prebiotics are not being studied in athletes. Many researchers reported the specific type of dietary components can do a measurable change in gut microbiota composition thereby increasing the levels of *Lactobacilli* and *Bifidobacteria* and many butyrate producing bacteria. The increase in *Lactobacilli* and *Bifidobacteria* can influence the immune functions, intestinal epithelium cell proliferation and protect individuals from oxidative stress induced due to the exercise [82]. Some of the studies reported that supplementation of polyphenol increased health promoting microbiota *Lactobacillus*, *Bifidobacterium*, and decreased pathogenic species *Clostridium* [83]. Roopchand [84] reported that polyphenols obtained from grape promote the growth of the gut bacterium *Akkermansia muciniphila* resulting in lower intestinal and systemic inflammation and improved metabolic system. These reported data can be a promised toward the various functional foods can regulate gut microbiome community, their structure and function

Exercise	Experimental design	Supplementation of Probiotic bacteria	Effect on GM	Remarks	References
Endurance trained men (triathletes, runners, cyclists)	Randomized, double-blinded, placebo controlled trial	<i>Bifidobacterium bifidum</i> W23, <i>Bifidobacterium lactis</i> W51, <i>Enterococcus faecium</i> W54, <i>Lactobacillus acidophilus</i> W22, <i>Lactobacillus brevis</i> W63, and <i>Lactococcus lactis</i> W58	—	Beneficially affected TNF- α and exercise induced protein oxidation	[75]
Athletes	Random trial	<i>L. rhamnosus</i> IMC 501® and <i>L. paracasei</i> IMC 502®	—	Increase antioxidant levels and neutralize the effects of reactive oxygen species.	[76]
Endurance Athletes	Randomized, double blind crossover study	<i>Lactobacillus Salivarius</i> (UCC118)	—	Attenuates exercise-induced intestinal hyperpermeability	[77]
Endurance Exercise (Swimming)	Random study	<i>Lactobacillus salivarius</i>	—	Improve muscle strength and endurance performance, increased hepatic and muscular glycogen storage, and decreased lactate, blood urea nitrogen (BUN), ammonia, and creatine kinase (CK) levels after exercise	[78]

Exercise	Experimental design	Supplementation of Probiotic bacteria	Effect on GM	Remarks	References
Treadmill exercise	Double-blind placebo-controlled clinical study.	<i>L. plantarum</i> TWK10	—	Physiological adaptation and health benefits for amateur runners	[59]
Treadmill exercise	Double-blind, placebo-controlled, crossover trial	<i>Lactobacillus fermentum</i> VRI-003	—	Enhance the mucosal immune system of elite athletes	[79]
Triathlon-high-intensity exercise	Double-blind experimental design	<i>Lactobacillus plantarum</i> PS128	Decreases: <i>Anaerotruncus</i> , <i>Caproiciproducens</i> , <i>Coprobacillus</i> , <i>Desulfovibrio</i> , <i>Dielma</i> , Family_ XIII, <i>Holdemania</i> , and <i>Oxalobacter</i>) Increases: <i>Akkermansia</i> , <i>Bifidobacterium</i> , <i>Butyricimonas</i> , and <i>Lactobacillus</i>	Ameliorate inflammation and oxidative stress, with improved exercise performance	[80]
Endurance exercise	Cross-over pilot study	SymbioLactComp® (<i>Lactobacillus paracasei</i> , <i>Lactobacillus acidophilus</i> , <i>Lactococcus lactis</i> and <i>Bifidobacterium animalis</i> subsp. <i>lactis</i>)	Increase: <i>Akkermansia muciniphila</i> , <i>Faecalibacterium prausnitzii</i> , <i>Bifidobacterium</i> spp.	Prevent intestinal or immune disorders	[81]

Table 1.
Effect of probiotics in trained individuals.

which will directly or indirectly contribute toward the health and performance of athletes. Also, protein diet supplementation, increased *Akkermansia muciniphila*, thereby influence host immunity and host metabolism in athletes [51].

5. Conclusion

Endurance exercise requires a considerable amount of energy, and when this energy cannot maintain a stable supply, it will lead to fatigue and reduce exercise performance. Endurance exercise has a profound impact on oxidative stress, intestinal permeability, muscle damage, systemic inflammation and immune response, dehydration. Gut microbiota promotes digestion and absorption of food to produce energy in host, thereby playing a great role on athlete’s energy consumption and exercise performance. There is a close interaction between exercise, microbiota and diet (**Figure 1**), the details warrant comprehensive investigations. Exercise, the proportion, timing and composition of the diet modulates the gut microbiota diversity. Better understanding, the impact of diet on gut microbiota and how gut microbiota respond to exercise, a nutritional strategy can be developed to modulate the gut microbiota diversity which can lead to enhanced the athlete’s overall performance and health.

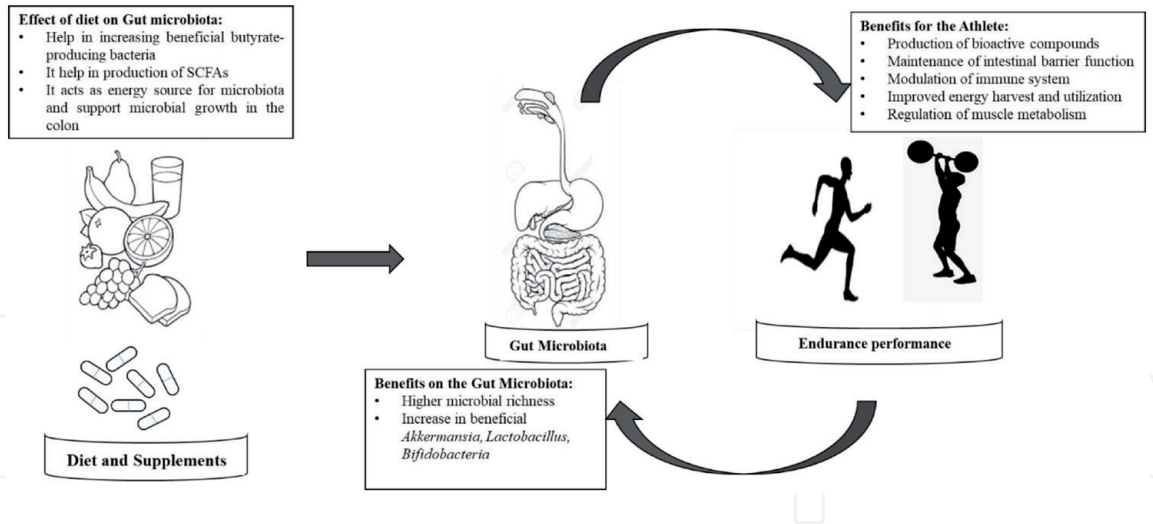


Figure 1.
Interaction between dietary components, gut microbiome, and endurance performance.

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Declaration of interests

We declare no competing interests.

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References

- [1] Schwellnus M, Kipps C, Roberts WO, Drezner JA, D'Hemecourt P, Troyanos C, et al. Medical encounters (including injury and illness) at mass community-based endurance sports events: an international consensus statement on definitions and methods of data recording and reporting. *Br J Sports Med*. 2019 Sep;53(17):1048-1055.
- [2] Rudolf V, Yulia D. Sport nutrition: the role of macronutrients and minerals in endurance exercises. 2018;
- [3] Baranauskas M, Stukas R, Tubelis L, Žagminas K, Šurkienė G, Švedas E, et al. Nutritional habits among high-performance endurance athletes. *Medicina (Kaunas)*. 2015;51(6):351-362.
- [4] Sillanpää E, Häkkinen A, Punnonen K, Häkkinen K, Laaksonen DE. Effects of strength and endurance training on metabolic risk factors in healthy 40-65-year-old men. *Scandinavian Journal of Medicine & Science in Sports*. 2009;19(6):885-895.
- [5] Tung Y-T, Hsu Y-J, Liao C-C, Ho S-T, Huang C-C, Huang W-C. Physiological and Biochemical Effects of Intrinsically High and Low Exercise Capacities Through Multiomics Approaches. *Front Physiol* [Internet]. 2019 Sep 18 [cited 2021 Apr 5];10. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6759823/>
- [6] Suzuki K. Cytokine Response to Exercise and Its Modulation. *Antioxidants (Basel)* [Internet]. 2018 Jan 17 [cited 2021 Apr 5];7(1). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5789327/>
- [7] Riede SJ, van der Vinne V, Hut RA. The flexible clock: predictive and reactive homeostasis, energy balance and the circadian regulation of sleep-wake timing. *J Exp Biol*. 2017 Mar 1;220(Pt 5):738-749.
- [8] Manichanh C, Borruel N, Casellas F, Guarner F. The gut microbiota in IBD. *Nat Rev Gastroenterol Hepatol*. 2012 Oct;9(10):599-608.
- [9] Monda V, Villano I, Messina A, Valenzano A, Esposito T, Moscatelli F, et al. Exercise Modifies the Gut Microbiota with Positive Health Effects. *Oxid Med Cell Longev* [Internet]. 2017 [cited 2021 Apr 5];2017. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5357536/>
- [10] Ticinesi A, Nouvenne A, Cerundolo N, Catania P, Prati B, Tana C, et al. Gut Microbiota, Muscle Mass and Function in Aging: A Focus on Physical Frailty and Sarcopenia. *Nutrients* [Internet]. 2019 Jul 17 [cited 2021 Apr 5];11(7). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6683074/>
- [11] Hughes RL. A Review of the Role of the Gut Microbiome in Personalized Sports Nutrition. *Front Nutr* [Internet]. 2020 Jan 10 [cited 2021 Apr 5];6. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6966970/>
- [12] Arumugam M, Raes J, Pelletier E, Le Paslier D, Yamada T, Mende DR, et al. Enterotypes of the human gut microbiome. *Nature*. 2011 May 12;473(7346):174-180.
- [13] Carding S, Verbeke K, Vipond DT, Corfe BM, Owen LJ. Dysbiosis of the gut microbiota in disease. *Microb Ecol Health Dis* [Internet]. 2015 Feb 2 [cited 2021 Apr 5];26. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4315779/>
- [14] Rogers GB, Keating DJ, Young RL, Wong M-L, Licinio J, Wesselingh S. From gut dysbiosis to altered brain function and mental illness: mechanisms and pathways. *Molecular Psychiatry*. 2016 Jun;21(6):738-748.

- [15] Schulz MD, Atay C, Heringer J, Romrig FK, Schwitalla S, Aydin B, et al. High-fat-diet-mediated dysbiosis promotes intestinal carcinogenesis independently of obesity. *Nature*. 2014 Oct 23;514(7523):508-512.
- [16] Sekirov I, Russell SL, Antunes LCM, Finlay BB. Gut microbiota in health and disease. *Physiol Rev*. 2010 Jul;90(3):859-904.
- [17] Delzenne NM, Neyrinck AM, Cani PD. Modulation of the gut microbiota by nutrients with prebiotic properties: consequences for host health in the context of obesity and metabolic syndrome. *Microbial Cell Factories*. 2011 Aug 30;10(1):S10.
- [18] Burcelin R. Gut microbiota and immune crosstalk in metabolic disease. *Molecular Metabolism*. 2016 Sep 1;5(9):771-781.
- [19] Keohane DM, Woods T, O'Connor P, Underwood S, Cronin O, Whiston R, et al. Four men in a boat: Ultra-endurance exercise alters the gut microbiome. *J Sci Med Sport*. 2019 Sep;22(9):1059-1064.
- [20] Thomas F, Hehemann J-H, Rebuffet E, Czjzek M, Michel G. Environmental and Gut Bacteroidetes: The Food Connection. *Front Microbiol* [Internet]. 2011 [cited 2021 Apr 5];2. Available from: <https://www.frontiersin.org/articles/10.3389/fmicb.2011.00093/full>
- [21] Proctor C, Thiennimitr P, Chattipakorn N, Chattipakorn SC. Diet, gut microbiota and cognition. *Metab Brain Dis*. 2017 Feb 1;32(1):1-17.
- [22] Shin N-R, Whon TW, Bae J-W. Proteobacteria: microbial signature of dysbiosis in gut microbiota. *Trends Biotechnol*. 2015 Sep;33(9):496-503.
- [23] Frank LK, Jannasch F, Kröger J, Bedu-Addo G, Mockenhaupt FP, Schulze MB, et al. A Dietary Pattern Derived by Reduced Rank Regression is Associated with Type 2 Diabetes in An Urban Ghanaian Population. *Nutrients*. 2015 Jul 7;7(7):5497-5514.
- [24] Schulze MB, Hoffmann K, Manson JE, Willett WC, Meigs JB, Weikert C, et al. Dietary pattern, inflammation, and incidence of type 2 diabetes in women. *Am J Clin Nutr*. 2005 Sep;82(3):675-684; quiz 714-5.
- [25] Murphy EF, Clarke SF, Marques TM, Hill C, Stanton C, Ross RP, et al. Antimicrobials: Strategies for targeting obesity and metabolic health? *Gut Microbes*. 2013 Feb;4(1):48-53.
- [26] Duncan SH, Belenguer A, Holtrop G, Johnstone AM, Flint HJ, Lobley GE. Reduced dietary intake of carbohydrates by obese subjects results in decreased concentrations of butyrate and butyrate-producing bacteria in feces. *Appl Environ Microbiol*. 2007 Feb;73(4):1073-1078.
- [27] Turnbaugh PJ, Ridaura VK, Faith JJ, Rey FE, Knight R, Gordon JI. The effect of diet on the human gut microbiome: a metagenomic analysis in humanized gnotobiotic mice. *Sci Transl Med*. 2009 Nov 11;1(6):6ra14.
- [28] Sánchez-Villegas A, Martínez-González MA, Estruch R, Salas-Salvadó J, Corella D, Covas MI, et al. Mediterranean dietary pattern and depression: the PREDIMED randomized trial. *BMC Medicine*. 2013 Sep 20;11(1):208.
- [29] Madsen L, Myrmet LS, Fjære E, Liaset B, Kristiansen K. Links between Dietary Protein Sources, the Gut Microbiota, and Obesity. *Front Physiol* [Internet]. 2017 Dec 19 [cited 2021 Apr 7];8. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5742165/>
- [30] Bibbò S, Ianaro G, Giorgio V, Scadaferri F, Masucci L, Gasbarrini A, et al. The role of diet on gut microbiota

composition. *Eur Rev Med Pharmacol Sci*. 2016 Nov;20(22):4742-4749.

[31] Araújo JR, Tomas J, Brenner C, Sansonetti PJ. Impact of high-fat diet on the intestinal microbiota and small intestinal physiology before and after the onset of obesity. *Biochimie*. 2017 Oct;141:97-106.

[32] Donati Zeppa S, Agostini D, Gervasi M, Annibalini G, Amatori S, Ferrini F, et al. Mutual Interactions among Exercise, Sport Supplements and Microbiota. *Nutrients*. 2019 Dec 20;12(1).

[33] Mika A, Van Treuren W, González A, Herrera JJ, Knight R, Fleshner M. Exercise Is More Effective at Altering Gut Microbial Composition and Producing Stable Changes in Lean Mass in Juvenile versus Adult Male F344 Rats. *PLoS One* [Internet]. 2015 May 27 [cited 2021 Apr 7];10(5). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4446322/>

[34] Marttinen M, Ala-Jaakkola R, Laitila A, Lehtinen MJ. Gut Microbiota, Probiotics and Physical Performance in Athletes and Physically Active Individuals. *Nutrients*. 2020 Sep 25;12(10).

[35] Wosinska L, Cotter PD, O'Sullivan O, Guinane C. The Potential Impact of Probiotics on the Gut Microbiome of Athletes. *Nutrients* [Internet]. 2019 Sep 21 [cited 2021 Apr 8];11(10). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6835687/>

[36] Christensen L, Roager HM, Astrup A, Hjorth MF. Microbial enterotypes in personalized nutrition and obesity management. *Am J Clin Nutr*. 2018 Oct 1;108(4):645-651.

[37] Zou H, Wang D, Ren H, Cai K, Chen P, Fang C, et al. Effect of Caloric

Restriction on BMI, Gut Microbiota, and Blood Amino Acid Levels in Non-Obese Adults. *Nutrients* [Internet]. 2020 Feb 27 [cited 2021 Apr 8];12(3). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146580/>

[38] Bressa C, Bailén-Andrino M, Pérez-Santiago J, González-Soltero R, Pérez M, Montalvo-Lominchar MG, et al. Differences in gut microbiota profile between women with active lifestyle and sedentary women. *PLoS One*. 2017;12(2):e0171352.

[39] Greenhill C. Gut microbiome influences exercise response. *Nat Rev Endocrinol*. 2020 Feb;16(2):68-69.

[40] Lee P, Yacyshyn BR, Yacyshyn MB. Gut microbiota and obesity: An opportunity to alter obesity through faecal microbiota transplant (FMT). *Diabetes Obes Metab*. 2019 Mar;21(3):479-490.

[41] Zhang T, Li Q, Cheng L, Buch H, Zhang F. *Akkermansia muciniphila* is a promising probiotic. *Microb Biotechnol*. 2019 Nov;12(6):1109-1125.

[42] Rivière A, Selak M, Lantin D, Leroy F, De Vuyst L. Bifidobacteria and Butyrate-Producing Colon Bacteria: Importance and Strategies for Their Stimulation in the Human Gut. *Front Microbiol*. 2016;7:979.

[43] Allen JM, Mailing LJ, Niemi GM, Moore R, Cook MD, White BA, et al. Exercise Alters Gut Microbiota Composition and Function in Lean and Obese Humans. *Med Sci Sports Exerc*. 2018 Apr;50(4):747-757.

[44] Gallè F, Valeriani F, Cattaruzza MS, Ubaldi F, Romano Spica V, Liguori G, et al. Exploring the association between physical activity and gut microbiota composition: a review of current evidence. *Ann Ig*. 2019 Dec;31(6):582-589.

- [45] Louis P, Flint HJ. Formation of propionate and butyrate by the human colonic microbiota. *Environ Microbiol*. 2017 Jan;19(1):29-41.
- [46] Scheiman J, Lubner JM, Chavkin TA, MacDonald T, Tung A, Pham L-D, et al. Meta-omics analysis of elite athletes identifies a performance-enhancing microbe that functions via lactate metabolism. *Nat Med*. 2019 Jul;25(7):1104-1109.
- [47] Donaldson GP, Lee SM, Mazmanian SK. Gut biogeography of the bacterial microbiota. *Nat Rev Microbiol*. 2016 Jan;14(1):20-32.
- [48] Morrison DJ, Preston T. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. *Gut Microbes*. 2016 May 3;7(3):189-200.
- [49] Sohail MU, Yassine HM, Sohail A, Al Thani AA. Impact of Physical Exercise on Gut Microbiome, Inflammation, and the Pathobiology of Metabolic Disorders. *Rev Diabet Stud*. 2019;15:35-48.
- [50] Yuan X, Xu S, Huang H, Liang J, Wu Y, Li C, et al. Influence of excessive exercise on immunity, metabolism, and gut microbial diversity in an overtraining mice model. *Scand J Med Sci Sports*. 2018 May;28(5):1541-1551.
- [51] Clark A, Mach N. Exercise-induced stress behavior, gut-microbiota-brain axis and diet: a systematic review for athletes. *Journal of the International Society of Sports Nutrition*. 2016 Nov 24;13(1):43.
- [52] Costa RJS, Snipe RMJ, Kitic CM, Gibson PR. Systematic review: exercise-induced gastrointestinal syndrome—implications for health and intestinal disease. *Alimentary Pharmacology & Therapeutics*. 2017;46(3):246-265.
- [53] Halvorsen FA, Lyng J, Glomsaker T, Ritland S. Gastrointestinal disturbances in marathon runners. *Br J Sports Med*. 1990 Dec;24(4):266-268.
- [54] van Wijck K, Pennings B, van Bijnen AA, Senden JMG, Buurman WA, Dejong CHC, et al. Dietary protein digestion and absorption are impaired during acute postexercise recovery in young men. *Am J Physiol Regul Integr Comp Physiol*. 2013 Mar 1;304(5):R356-R361.
- [55] Nadatani Y, Watanabe T, Shimada S, Otani K, Tanigawa T, Fujiwara Y. Microbiome and intestinal ischemia/reperfusion injury. *J Clin Biochem Nutr*. 2018 Jul;63(1):26-32.
- [56] Morishima S, Aoi W, Kawamura A, Kawase T, Takagi T, Naito Y, et al. Intensive, prolonged exercise seemingly causes gut dysbiosis in female endurance runners. *Journal of Clinical Biochemistry and Nutrition*. 2020;advpub.
- [57] Heiss CN, Olofsson LE. Gut Microbiota-Dependent Modulation of Energy Metabolism. *JIN*. 2018;10(3):163-171.
- [58] Barton W, Penney NC, Cronin O, Garcia-Perez I, Molloy MG, Holmes E, et al. The microbiome of professional athletes differs from that of more sedentary subjects in composition and particularly at the functional metabolic level. *Gut*. 2018 Apr;67(4):625-633.
- [59] Chen Y, Liao C, Huang Y, Chen M, Huang C, Chen W, et al. Proteome and microbiota analysis highlight *Lactobacillus plantarum* TWK10 supplementation improves energy metabolism and exercise performance in mice. *Food Sci Nutr*. 2020 Jun 3;8(7):3525-3534.
- [60] Shephard RJ, Shek PN. Potential impact of physical activity and sport on the immune system--a brief review. *Br J Sports Med*. 1994 Dec;28(4):247-255.

- [61] Goldszmid RS, Dzutsev A, Trinchieri G. Host Immune Response to Infection and Cancer: Unexpected Commonalities. *Cell Host & Microbe*. 2014 Mar 12;15(3):295-305.
- [62] Pedersen BK, Toft AD. Effects of exercise on lymphocytes and cytokines. *Br J Sports Med*. 2000 Aug;34(4):246-251.
- [63] Maslowski KM, Mackay CR. Diet, gut microbiota and immune responses. *Nature Immunology*. 2011 Jan;12(1):5-9.
- [64] Ji LL. Antioxidants and Oxidative Stress in Exercise. *Proceedings of the Society for Experimental Biology and Medicine*. 1999;222(3):283-292.
- [65] Ji L. Oxidative stress during exercise: Implication of antioxidant nutrients. *Free Radical Biology and Medicine*. 1995 Jun 1;18(6):1079-1086.
- [66] Xu J, Xu C, Chen X, Cai X, Yang S, Sheng Y, et al. Regulation of an antioxidant blend on intestinal redox status and major microbiota in early weaned piglets. *Nutrition*. 2014 May;30(5):584-589.
- [67] Ghosh S, Dai C, Brown K, Rajendiran E, Makarenko S, Baker J, et al. Colonic microbiota alters host susceptibility to infectious colitis by modulating inflammation, redox status, and ion transporter gene expression. *Am J Physiol Gastrointest Liver Physiol*. 2011 Jul;301(1):G39-G49.
- [68] Antonio J, Kalman D, Stout JR, Greenwood M, Willoughby DS, Haff GG, editors. *Essentials of Sports Nutrition and Supplements* [Internet]. Humana Press; 2008 [cited 2021 Apr 10]. Available from: <https://www.springer.com/gp/book/9781588296115>
- [69] Colgan SP. Swimming through the gut: Implications of fluid transport on the microbiome. *Dig Dis Sci*. 2013 Mar;58(3):602-603.
- [70] Musch MW, Wang Y, Claud EC, Chang EB. Lubiprostone Decreases Mouse Colonic Inner Mucus Layer Thickness and Alters Intestinal Microbiota. *Dig Dis Sci*. 2013 Mar;58(3):668-677.
- [71] Qiao Y, Sun J, Ding Y, Le G, Shi Y. Alterations of the gut microbiota in high-fat diet mice is strongly linked to oxidative stress. *Appl Microbiol Biotechnol*. 2013 Feb;97(4):1689-1697.
- [72] Tremaroli V, Bäckhed F. Functional interactions between the gut microbiota and host metabolism. *Nature*. 2012 Sep;489(7415):242-249.
- [73] Gatlin DM, Peredo AM. Prebiotics and probiotics: definitions and applications. *Prebiotics and probiotics: definitions and applications* [Internet]. 2012 [cited 2021 Apr 10];(No.4711). Available from: <https://www.cabdirect.org/cabdirect/abstract/20133083066>
- [74] Pyne DB, West NP, Cox AJ, Cripps AW. Probiotics supplementation for athletes - clinical and physiological effects. *Eur J Sport Sci*. 2015;15(1):63-72.
- [75] Lamprecht M, Bogner S, Schippinger G, Steinbauer K, Fankhauser F, Hallstroem S, et al. Probiotic supplementation affects markers of intestinal barrier, oxidation, and inflammation in trained men; a randomized, double-blinded, placebo-controlled trial. *J Int Soc Sports Nutr*. 2012 Sep 20;9(1):45.
- [76] Martarelli D, Verdenelli MC, Scuri S, Cocchioni M, Silvi S, Cecchini C, et al. Effect of a probiotic intake on oxidant and antioxidant parameters in plasma of athletes during intense exercise training. *Curr Microbiol*. 2011 Jun;62(6):1689-1696.
- [77] Brennan C, Axelrod C, Paul D, Hull M, Kirwan J. Effects Of A Novel Probiotic On Exercise-Induced Gut Permeability and Microbiota in Endurance Athletes. 2018.

[78] Lee M-C, Hsu Y-J, Ho H-H, Hsieh S-H, Kuo Y-W, Sung H-C, et al. *Lactobacillus salivarius* Subspecies *salicinius* SA-03 is a New Probiotic Capable of Enhancing Exercise Performance and Decreasing Fatigue. *Microorganisms* [Internet]. 2020 Apr 9 [cited 2021 Apr 10];8(4). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7232535/>

[79] Cox AJ, Pyne DB, Saunders PU, Fricker PA. Oral administration of the probiotic *Lactobacillus fermentum* VRI-003 and mucosal immunity in endurance athletes. *Br J Sports Med*. 2010 Mar;44(4):222-226.

[80] Huang W-C, Pan C-H, Wei C-C, Huang H-Y. *Lactobacillus plantarum* PS128 Improves Physiological Adaptation and Performance in Triathletes through Gut Microbiota Modulation. *Nutrients*. 2020 Aug 1;12(8).

[81] Schmitz L, Ferrari N, Schwiertz A, Rusch K, Woestmann U, Mahabir E, et al. Impact of endurance exercise and probiotic supplementation on the intestinal microbiota: a cross-over pilot study. *Pilot Feasibility Stud*. 2019;5:76.

[82] Gleeson M, Bishop NC, Oliveira M, Tauler P. Daily probiotic's (*Lactobacillus casei* Shirota) reduction of infection incidence in athletes. *Int J Sport Nutr Exerc Metab*. 2011 Feb;21(1):55-64.

[83] Ma G, Chen Y. Polyphenol supplementation benefits human health via gut microbiota: A systematic review via meta-analysis. *Journal of Functional Foods*. 2020 Mar 1;66:103829.

[84] Roopchand DE, Carmody RN, Kuhn P, Moskal K, Rojas-Silva P, Turnbaugh PJ, et al. Dietary Polyphenols Promote Growth of the Gut Bacterium *Akkermansia muciniphila* and Attenuate High-Fat Diet-Induced Metabolic Syndrome. *Diabetes*. 2015 Aug;64(8):2847-2858.