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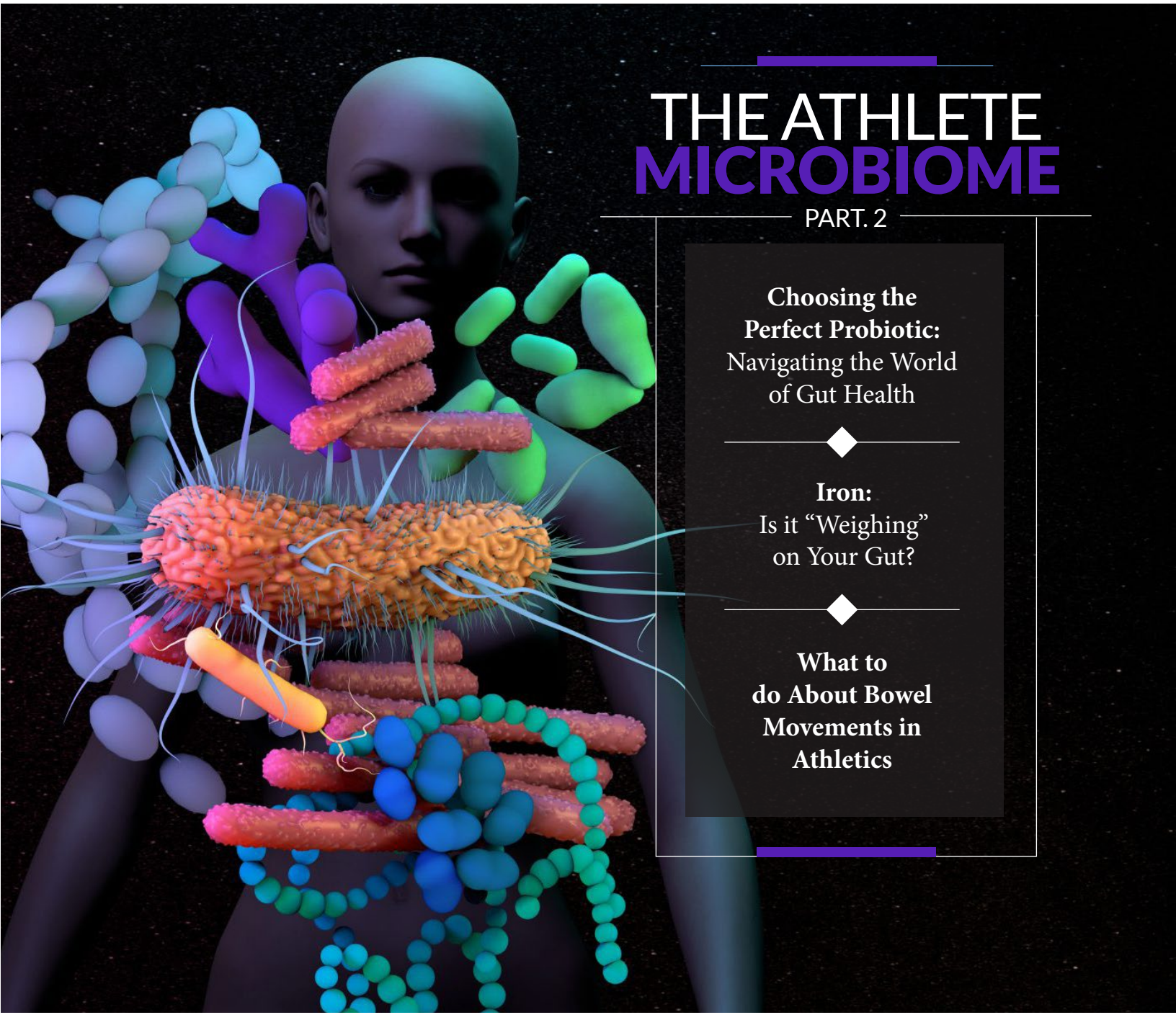

THE ATHLETE MICROBIOME

PART. 2

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Pharmacist Athlete Contributors

Dr. Matthew Liaw, PharmD.

Dr. Jessica Beal-Stahl, PharmD.

Dr. Scott Kjelson, PharmD.

Dr. Brandon K. Welch, PharmD., CWC

Dr. Marissa Brooks, PharmD., MBA, CWC

Dr. Kristal Potter, Capt, USAF, BSC, PharmD.

Dr. Hussam Hamoush, PharmD

Sean Casey, RD, CSCS

Robert P. Nickell, Rph.

Dr. Taylor Gardner, PharmD.

MISSION STATEMENT

THE PURPOSE

Brandon K. Welch, Pharm.D.
Founder of Pharmacy Athlete

The Sports Pharmacy magazine exists to empower a community of pharmacist professionals to optimize their impact through disseminating evidence-based knowledge and applied science on sports performance supplements and nutrition. Pharmacists can be pivotal players in the arena of sports. They are poised to help intersect biochemistry with biomechanics and real-life science with athletic performance. Our patient athletes rely on results and we are here to deliver them in real-time.

> Where Pharmacists merge Metabolic Health with Peak Human-Performance
>
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Choosing the Perfect Probiotic

Navigating the World of Gut Health

By Nicole Jameson

AUTHORS BIO:

Nicole Jameson is a fourth year PharmD student at Northeastern University. Nicole holds a Bachelor's degree in Exercise Physiology, which complements her passion for healthcare and well-being. Throughout her academic journey, Nicole has developed an interest in the areas of oncology and ambulatory care. Her unwavering commitment to patient care and improving health outcomes has fueled her desire to pursue a residency upon graduation. Beyond her academic pursuits, Nicole has a diverse range of hobbies that bring balance to her life. She enjoys cooking, participating in CrossFit competitions, golfing, and spending quality time with family and friends. Nicole envisions a career where she can combine her knowledge of pharmacotherapy and patient care with her passion for holistic wellness and promoting an active lifestyle.

Imagine this scenario: You are prescribed an antibiotic, and your doctor advises you to take it with a probiotic for optimal gut health. Amidst the plethora of options, how can you confidently choose the right one? Welcome to the fascinating world of probiotics – where these beneficial microorganisms hold the power to revolutionize your gut health.

Probiotics are referred to as "good bacteria." Over recent years, they have garnered considerable interest for their ability to promote a healthy gut and offer a wide range of health benefits for individuals of all ages.[1] The complexity of probiotics lies in the fact that there are thousands of unique bacterial "strains" that can be used for specific conditions.[1]

In this introduction to probiotics, we will provide insights into the pressing query of selecting the ideal probiotic, help you understand the significance of different strains, equip you with the knowledge to make an informed decision, and empower you to choose the perfect probiotic tailored to you during your health journey!

The Role of Gut Microbiome in Overall Health

The human digestive tract and its associated microbes are called the *gut microbiome*.[2] The relationship between gut microbiota and human health is well established within the scientific community.[3] It has been recognized that the gut microbiota not only plays a significant role in maintaining gut health as a whole but is also associated with various diseases ranging from inflammatory bowel diseases (IBD) and irritable bowel syndrome (IBS) to mood disorders. However, more clinical evidence is needed to support this fully.[2] Probiotics can be advantageous in providing extra support when there is gut dysbiosis, an imbalance of microorganisms in the digestive system, which can manifest in a variety of ways.[2]

Understanding Probiotics

Probiotics are living microorganisms that offer potential health benefits when ingested.[4] They are present in yogurts, fermented foods, and dietary supplements. While bacteria and other microorganisms can often be perceived as detrimental, numerous strains are beneficial. Certain bacteria aid food digestion, eliminate harmful cells, and generate essential vitamins. The microorganisms found in probiotic products closely resemble or are identical to the ones naturally residing in our bodies.[4]

Probiotic products can comprise a diverse range of microorganisms.[4] The most common are bacteria that belong to groups known as *Lactobacillus* and *Bifidobacterium*. Other bacteria and even yeasts, such as *Saccharomyces,* can serve as probiotics. It is important to note that various strains of probiotics can yield distinct effects, which may be beneficial for certain health conditions.[4]

Factors to Consider When Choosing a Probiotic

When choosing a probiotic, it is important to consider colony-forming units (CFUs) or the number of bacteria per dose, the types of strains used and their clinical level of effectiveness, and how your probiotics need to be stored.[5] Generally, it is best to choose a probiotic with at least 1 billion CFUs containing the genus *Lactobacillus, Bifidobacterium, Bacillus,* or *Saccharomyces*

Indigestion is characterized by discomfort in the upper abdomen, acid reflux, flatulence, and belching.

boulardii, some of the most researched probiotics. However, each genus of bacteria encompasses numerous strains that may produce different results, which will be discussed in further detail. It is also important to note storage conditions, some are room temperature, and others require refrigeration. Generally, refrigeration is recommended as some strains may be sensitive to heat. Additionally, it is advisable to seek out a probiotic encapsulated with a food source, such as inulin, so that the bacteria have something to feed off and thus remain viable on the shelf. Lastly, paying attention to the expiration date is important to ensure the best effectiveness.[5]

Common Health Conditions and Corresponding Probiotic Strains

Common health conditions, including indigestion, IBS, stress, anxiety, and the use of antibiotics, can disrupt the balance of good and bad bacteria in your gut.[6] Let's dive deeper into these conditions and which probiotic strains may benefit each.

Digestive Health & Gastrointestinal Conditions

Indigestion is characterized by discomfort in the upper abdomen, acid reflux, flatulence, and belching.[6] Similarly, IBS is characterized by symptoms of abdominal discomfort and altered bowel habits that occur over at least three months. Although the cause of IBS remains unknown, evidence has linked it to intestinal microbiota and overgrowth of bacteria. There have been several clinical trials investigating the use of probiotics for IBS, with less clinical evidence available to support the use of probiotics for upper digestive tract conditions like indigestion.[6]

Although clinical studies involving probiotics have primarily focused on the lower digestive tract, a systematic review by Cheng and Ouwehand evaluated 13 clinical studies to determine the potential of probiotics to alleviate upper gastrointestinal symptoms in the general adult population. They found that the greatest improvements in acid reflux and abdominal pain were seen in the groups who were treated with multi-strain products containing various strands in species of *Bifidobacterium bifidum, Bifidobacterium lactis, Lactobacillus casei, Lactobacillus plantarum, Lactobacillus rhamnosus,* and *Lactobacillus acidophilus.* These findings are consistent with data that supports that these strains may be beneficial in supporting a healthy digestive tract.[6]

As mentioned previously, numerous clinical trials have explored the

therapeutic potential of probiotics as therapy for IBS.[7] One study in a meta-analysis of 3 randomized controlled trials found significant reductions in pain, bloating, and bowel movement difficulty with the use of *Bifidobacterium infantis* when compared to a *lactobacillus* species. Similarly, in a larger follow-up study, reduction in pain and relief of IBS symptoms were noted in the high-dose group containing 1×10^{10} CFU/mL of *B. infantis* compared to placebo. While the available evidence is not robust enough to endorse the general recommendation of probiotics for IBS, the potential benefits seem to be most pronounced when utilizing combination products containing *bifidobacteria* species instead of individual *lactobacillus* probiotics.[7]

Antibiotic-Associated GI Upset

When prescribed antibiotics, it is common to take a probiotic supplement to help rebalance the gut microbiome.[8] Antibiotic-associated diarrhea (ADD) is a frequently observed adverse effect of antibiotic use with a prevalence of between 5 to 35%, depending on the type of antibiotic. A noteworthy meta-analysis conducted in 2012 determined that probiotics could decrease the likelihood of experiencing side effects associated with antibiotic use by 64%. It is crucial to choose the right strains of probiotics to ensure they will survive when taken with antibiotics to exert the best effects.[8]

While past research recommends waiting until after antibiotics are finished to start taking probiotics, current research does not support this.[8] Over recent years, extensive clinical research suggests the most suitable approach for probiotic supplementation during antibiotic therapy involves specific strains consumed concurrently with antibiotics instead of separate administration. These strains include *Lactobacillus acidophilus* Rosell-52, *Lactobacillus rhamnosus* Rosell-11, and *Bifidobacterium lactis* Lafti B94. These well-studied strains can be taken safely at the same time as antibiotics, as they have been shown to survive stomach acid, which is not the case for many strains of probiotics.[8]

Recommended use for a supplement containing these strains are as follows:[8]

> **By modulating the gut microbiota, probiotics can aid in disease states, including IBS, indigestion, mental health conditions, during antibiotic therapy to promote healthy bowel movements, and contribute to mood stability.**

- Take one capsule daily with breakfast, even with your antibiotic medication.
- Take daily until the antibiotic course is finished, and continue preferably for one week after.

However, in the case of using different strains, it is advisable to maintain a two-hour interval between antibiotic administration and the consumption of a probiotic supplement. This gap allows for the avoidance of potential drug-drug interactions.[8]

Stress, Mood, & Mental Health Conditions

In recent years, there has been a significant surge in research exploring the concept of the gut-brain axis, which investigates the relationship between our gut and emotions and how the microbial composition in our intestines can influence our mood.[9] Specific strains of probiotics have shown the ability to impact our mood positively. These strains are sometimes referred to as 'psychobiotics'.[9]

There are specific probiotic strains of interest that have been extensively studied for their effects on stress, anxiety, and low mood, which include *Bifidobacterium longum* 1714, *Lactobacillus acidophilus* Rosell-52, *Bifidobacterium longum* Rosell-175, and *Lactobacillus casei* Shirota.[9] A recent notable study provides compelling findings in which individuals who consumed 1 billion CFU of *Bifidobacterium longum* 1714 reported a reduction in daily stress levels compared to placebo. Although further clinical studies are needed to assess which strains may be best for managing stress and well-being, recent data on probiotic strains mentioned looks promising.[9]

Go With Your Gut

In summary, probiotics offer a valuable means to modulate the gut microbiota effectively.[10] By modulating the gut microbiota, probiotics can aid in disease states, including IBS, indigestion, mental health conditions, during antibiotic therapy to promote healthy bowel movements, and contribute to mood stability.[10] When making probiotic selections, individuals can utilize clinical evidence as a trustworthy resource to inform their choices regarding strains that may demonstrate higher effectiveness for specific conditions. It is always advisable to seek guidance from your healthcare provider before incorporating probiotics into your daily regimen.

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NSAIDs
An Athlete's Holy Grail

By Mayte Lezcano

AUTHOR BIO:

Mayte Lezcano is a fourth year student in the Pharm. D. program at Nova Southeastern University (NSU), Fort Lauderdale campus. She was born and raised in Miami, Florida and graduated from Gulliver Preparatory School in 2017. Mayte formerly attended NSU as an undergraduate where she acquired a Bachelor of Science degree in Biology within three years. During her time at NSU, she had the opportunity to play collegiate softball under an athletic scholarship. In May 2020, Mayte was inducted into Chi Alpha Sigma, honor society that honors student-athletes who have excelled in both the classroom and in athletic competition. She is still a part of the softball program at NSU and was granted an extra year of eligibility since COVID-19 unexpectedly terminated her season due to health precautions in the spring of 2020. Mayte's competitive nature and dedication stems from her seventeen years of athletic experience. She believes her commitment, ability to strive under pressure, and quick adjustments to constructive criticism will be an asset on her journey to her professional endeavors and that these elements parallel from the playing field to the health care system harmoniously. Mayte is a major advocate of being a part of something that is bigger than herself. She currently president of the Rho Chi Pharmacy Honor Society, representing the top 20% of her class. She was also inducted into the Phi Kappa Phi Honor society in Winter 2021 after earning a seat in all consecutive academic Chancellor's List. On her spare time, she enjoys working out and maintaining a healthy lifestyle.

Introduction

As an athlete, there is a constant grind to ensure the body is prepared for competition. A critical component of that aspect is recovery. Even with proper supplementation, there has come a point in every person's life where they search for the ibuprofen bottle at the last minute to reduce pain and inflammation brought on by strenuous training or injury. But, just as anything we put into our bodies alters the metabolic processes within, so do nonsteroidal anti-inflammatory drugs, *especially* in the gut. The gut microbiome is composed of a diverse group of microorganisms that contribute to the metabolism and absorption of food and medicines. There is promising research demonstrating how the choice of NSAID is susceptible to a distinct subset of microbial population growth. This article highlights the fascinating phenomenon of NSAIDs' effect on the gut microbiome and how we can optimize its use to benefit a population where health is a priority.

NSAIDs: An Athlete's Holy Grail

Athletes are, by definition, the epitome of physical performance. While they undergo extraordinary lengths to prepare their body for competition, obstacles such as injury and fatigue get in the way of performing to the best of their abilities. Many athletes rely on nonsteroidal anti-inflammatory drugs (NSAIDs) to compensate for the strenuous training they complete as a means to recovery. No, not steroids as in performance enhancing testosterone, but those naturally occurring within the adrenocorticoid steroidal system in our bodies like prednisone. Examples of NSAIDs include Bayer® (aspirin), Advil® (ibuprofen), and Aleve® (naproxen). Sound familiar? Its popularity is because they are easily accessible and affordable over-the-counter, generally well tolerated, and proven efficacious for temporary pain relief with their anti-inflammatory pharmacologic effects.

NSAIDs work by decreasing pain, inflammation, and typically associated fever. Diving in pharmacologically, they are inhibitors of cyclooxygenase (COX) enzymes and cascading prostaglandin synthesis.[1] There is an interplay with NSAIDs with COX-1 and COX-2 enzymes. More specifically, COX-1 enzymes are responsible for maintaining homeostatic functions within the body, while COX-2 enzymes form the prostaglandins that modulate inflammation and pain. NSAIDs are classified on their selectivity for COX inhibition. For example, ibuprofen is a non-selective COX inhibitor, potentially expressing more adverse effects on the body than celecoxib would, which is selective for COX-2 inhibition.

Unfortunately, the caveat is that cyclooxygenases are also responsible for producing certain prostaglandins that protect wall linings within the intestines that aid in the

protection against peptic ulcer disease. These same COX enzymes also produce thromboxane, which aids in blood clotting. For those reasons, NSAIDs are also infamously known to exhibit gastrointestinal and cardiovascular adverse effects.[1] Adverse effects include internal gastrointestinal (GI) bleeding, ulcer-producing risks, and increases in blood pressure—much more than your typically upset stomach complaint. More extreme effects are dose and duration dependent. Besides, they are commonly used amongst all patient populations regardless due to their accessibility and clinical effectiveness in recovery and the management of medical conditions such as gout and arthritis. Preferred NSAIDs are based on their selectivity to minimize the risk of associated adverse effects.

It's a Bug's Life

Our body houses countless species of bacteria that coexist with one another in a symbiotic relationship. The GI tract is a complex entity, varying in nutrients, tissues, and microorganisms. Therefore, the GI tract determines the dominant microbiota throughout localized compartments within the abdomen and its effect on metabolic processes. Organisms collectively within the gut that compose the gut microbiome include bacteria, fungi, and viruses. Healthy human gut flora is quite diverse and primarily consists of seven main phyla: *Bacteroidetes*, *Firmicutes, Proteobacteria, Verrumicrobia, Actinobacteria*, *Fusobacteria, and Cyanobacteria*.[1] These hard-to-pronounce species are the endgame determinants of a healthy gut and do so within the intestinal lining of the wall, aiding in food digestion, drug absorption, and fortifying immune defenses. The further down the intestines we travel, the less accessibility bacteria have to oxygen, making it susceptible to colonization of anaerobic bacteria such as *Bacteroidaceae, Prevotellaceae, Rikenellaceae, Lachnospiraceae*, and *Ruminococcaceae.*[1] It is when the host (our) defense systems are faulty due to disease, malnutrition, or drug metabolism and toxicity that makes our bodies susceptible to colonization and infection.

NSAIDs and the Gut Microbiome

Unsurprisingly, gut microbes are largely affected by synthetic entities, also known as xenobiotics. Xenobiotics are outside substances that are unknown and unrecognized by the body. Studies are now investigating the biodiversity and composition of the gut microbiome after specific medication use. Just as the GI tract reflects the medication and its impact on metabolic processes, the bacterial growth within the intestines also reflects the choice of NSAID utilized.[2] Although not a completely defined phenomenon, there is promising research that each type of NSAID used is susceptible to a distinct subset of microbial population growth. Host-gut microbiota interactions influence NSAID distribution, therapeutic efficacy, and toxicity.[1] It all has to do with the balance between pharmacokinetics (i.e., metabolism: what the body does to the drug) and pharmacodynamics (i.e., adverse effects: drug effects on the body).

One specific study evaluated NSAID use within the past 30 days in 155 adults where individual stool specimens were submitted for analysis.[2] The research pinpointed a correlation between the use of NSAIDs and the effect it has on gut microbiota. They can directly impact the composition and function of the gut microbiota or indirectly alter the gut's physiological properties, which may create an imbalance of flora known as dysbiosis.[2] There were differences in the relative abundance of specific bacteria for individuals who took a single drug versus individuals who used drug combinations and those who did not use any medications. Ultimately, the number of drugs did not significantly impact gut biodiversity, but the specific types of medications did.[2] Please refer below to a summary of microbial enrichment of specific NSAIDs compared to non-medication users.

Drug	Associated Microbial Growth
Aspirin	*Prevotella* spp., *Bacteroides* spp., family *Ruminococcaceae,* and *Barnesiella* spp.
Celecoxib	*Acidaminococcaceae, Enterobacteriaceae*
Ibuprofen	*Acidaminococcaceae, Enterobacteriaceae*
Ibuprofen vs naproxen	*Propionibacteriaceae, Pseudomonadaceae, Puniceicoccaceae, Rikenellaceae*
NSAIDs + proton-pump inhibitors (PPIs)	*Bacteroides* spp., E*rysipelotrichaceae* spp.
NSAIDs + antidepressants + laxatives	*Ruminococcaceae*

Go With Your Gut

Many lifestyle modifications can be made to promote gut health. A few are listed below:

NSAID Utilization -

To minimize the risk of gut malnutrition, NSAIDs should be restricted to the lowest effective doses and shortest duration of therapy when possible to avoid susceptibility of unwanted bacterial growth and associated long-term adverse effects. Voltaren® (diclofenac) is an alternative anti-inflammatory topical gel that only has up to 6% system absorption from the skin when used locally. Diclofenac differs from your typical IcyHot® in that it focuses specifically on reducing joint pain, while the latter is a temporary anesthetic with temperature cooling properties.

Nutrition -

Apart from optimizing dose and duration with NSAID use, there are certain superfoods that individuals can add to their daily diet to promote gut health, such as:

- Turmeric and its active ingredient, curcumin: a spice intentionally fabricated with black pepper to aid in intestinal digestion
- Ginger: a natural spice containing antioxidant, anti-inflammatory, and anti-ulcer producing effects
- Omega 3 fatty acids: expression of EPA and DHA, expressing anti-inflammatory properties
- Fiber: vegetables, legumes, beans, and citrus fruit affect the rate of digestion of foods, the absorption of nutrients, and the movement of waste through the colon
- Fermented foods: yogurt, kimchi, sauerkraut, and kombucha containing live cultures of microorganisms to colonize and fortify the gut microbiome
- Prebiotic foods: foods rich in fiber that gut microbiota thrive on to support the beneficial properties of those microorganisms
- Polyphenol-rich foods: Cocoa and dark chocolate, red wine, grape skins, green tea, and almonds rich in antioxidants

Probiotics -

Probiotics are active microorganisms within food or supplements intended to help maintain and restore natural beneficial gut flora composition. Probiotics can inhibit the colonization of pathogenic bacteria in the intestine, build a healthy intestinal mucosa protective layer, and enhance the host immune system.[4] Common probiotics are Florastor ® and Florajen® with live cultures of *Lactobacillus* or *Bifidobacterium*, prime examples of bacteria known to aid the body's gut microbiome. Daily supplementation with probiotics helps combat the disadvantages of unwanted colonization of "bad" bacteria that typically cause bloating, indigestion, and diarrhea from malnutrition or susceptibility to drug usage. NSAIDs and antibiotics are classically known to alter the gut flora. Yes, antibiotics aid in fighting bacterial infection but also come with adverse effects like GI upset and diarrhea because they completely wipe all bacteria within the gut, just as alcohol hand sanitizer kills most "good" and "bad" microorganisms on the skin's surface. In the end, probiotics are an effective method to improve hut health and immunity.

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Iron:
Is it "Weighing" on Your Gut?

By Dr. Taylor Gardner, Pharm.D

AUTHOR BIO:

Dr. Gardner is a former college athlete and fitness enthusiast. She is the Wellness Pharmacist for Stonebriar Pharmacy. Taylor is committed to her patient's health and wellness through diet, exercise, daily habits, supplements, and pharmaceutical intervention.

While most female athletes are "pumping iron" to help achieve their athletic goals, many forget about the type of iron that is vital for reaching the performance goals they are chasing. Iron deficiency in physically active females has been a hot topic over the last several decades, as it is suggested that up to 25% of female athletes are iron deficient.[1] Yet, when it comes to iron supplementation, it can be a punch in the gut, literally. Nausea, bloating, and constipation are the unpleasant side effects of oral iron supplements that can be felt, but these supplements are also causing negative changes within our gut microbiome. While too little iron could prevent female athletes from achieving top athletic performance, too much iron could lead to gut wrenching performance results.

Let's Talk About Iron

Iron is a micronutrient that is essential for growth and development, supporting the function of proteins and enzymes in maintaining physical and cognitive development.[2] The human body uses iron to make hemoglobin and myoglobin, proteins that play a vital role in oxygen transportation and the generation of energy within the body.[3] As iron stores in the body become depleted, the body's ability to move oxygen can be compromised, placing an athlete at risk for decreased endurance, muscle function, and work capacity.[4]

The two main forms of iron are heme and nonheme. Heme iron is found in animal sources including meat, seafood and poultry, whereas nonheme iron can be found in nuts, beans, vegetables and iron-fortified foods.[3] Ascorbic acid, meat, poultry and seafood can enhance the absorption of nonheme iron, while phytate (found in grains and beans) and certain polyphenols (found in some cereals and legumes) have the opposite effect.[3] Calcium can also reduce the bioavailability of both heme and nonheme iron and while not definitively established, it is suggested to avoid taking calcium and iron supplements together.[3]

The way in which the body handles iron can be thought of as a seesaw, constantly working to maintain the balance between the current iron stores and iron consumed in the diet. The human body does not have a direct mechanism for iron excretion. Therefore, it relies on hepcidin, a circulating peptide hormone, to regulate iron absorption and distribution throughout the body.[3,5]

Symptoms of Iron Deficiency

While several factors can influence an athlete's performance, iron should be one of the first things considered when fatigue and performance-related concerns are mentioned. In addition to fatigue and slower recovery after workouts, reduced immune function, pale skin, shortness of breath, headaches, dizziness, and heart palpitations may suggest iron deficiency.[6] Iron deficiency is diagnosed with a serum ferritin test that measures the amount of iron stored in the body. A serum concentration lower

than 30mcg/L suggests iron deficiency, while a value lower than 10mcg/L suggests iron deficiency anemia.[7]

Why Female Athletes are at Higher Risk

Any athlete functioning at a high capacity will increase their requirement for micronutrients, such as iron, due to high cellular turnover and tissue repair within the body.[4] While iron deficiency should be taken seriously in any patient, physically active females and endurance athletes have been a topic of considerable attention over the last few decades.[1] Females specifically are at a greater risk for compromised iron status primarily due to monthly menstrual cycles and insufficient dietary iron intake through elimination diets and/or vegetarian and vegan diets.[8] Increased iron losses associated with foot strike hemolysis, heavy sweating, increased blood loss through the urine and gastrointestinal (GI) tract, and exercise-induced acute inflammation can also increase the risk of iron deficiency in female athletes.[9]

Improving Iron Through Diet

Improving iron stores through dietary modifications is the preferred strategy for ensuring adequate iron intake and maintaining iron stores in iron-deficient females.[1,10] However, achieving adequate intake through the diet alone can be challenging given dietary restrictions and preferences, thus producing mixed results in effectiveness.[11] The recommended dietary allowance (RDA) in the United States for adult females is set at 18mg of iron per day, and even higher in vegetarians as only non-heme iron is consumed.[10] While not an official recommendation, some authors suggest that iron requirements for female endurance athletes, particularly distance runners, are increased by approximately 70%.[10] If this suggestion were followed, our female athletes' current iron RDA would be significantly higher.

The dietary modification should be centered around healthy eating practices, focusing on increasing total daily iron through both heme and non-heme iron.[1] While the majority of iron in the Western diet comes from non-heme iron, heme iron sources should be prioritized if available due to better absorption by the body (up to 40%) compared to non-heme (2-20%).[11] Focus should be on consuming dietary iron with fruits and vegetables high in vitamin C and avoiding foods that may decrease iron absorption.

Pharmacologic Intervention: Oral Iron Supplementation

If iron levels cannot be improved through dietary changes, alternate forms of iron supplementation should be considered under a healthcare provider's direct supervision and guidance. Oral iron is effective in treating iron deficiency due to its low cost, high bioavailability, and effectiveness.[5] Oral ferrous sulfate is the most common oral iron supplement, taken two to three times per day.[12] Each 200mg tablet contains 65mg of elemental iron, totaling a daily maximum elemental iron dose of 195mg.[12] While effective, the limiting factor of oral iron is unpleasant side effects, including abdominal discomfort, constipation, nausea, and bloating.[12] Through research, oral iron supplementation has also shown negative effects on the gut microbiome.[5] The direct mechanism of how iron causes these negative GI side effects is largely unknown.[13] Yet we know that iron supplements contain significantly more elemental iron than can be absorbed by the body. As a result, large amounts of unabsorbed iron are left in the lumen of the GI tract, affecting the gut microbiome through increased levels of certain enteropathogens and decreased protective species such as lactobacilli.[5]

Combating Negative Effects of Oral Iron:

Up to 60% of individuals taking oral iron supplements experience GI effects, leading to noncompliance in many of these patients.[14] While more research is needed to determine the exact mechanism of why and how oral iron causes these unpleasant GI side effects,[5] there are some suggested methods that patients can implement that may improve their tolerability.

Combining pre- and probiotics with iron supplementation may help mitigate iron-induced microbiome changes.[5] Lactic acid,

produced by lactobacilli, increases the dietary bioavailability of iron.[15] Thus, probiotics with *Lactobacillis fermentum* may help reduce the GI side effects of oral iron by increasing the amount of iron absorbed in the GI tract.[16] Studies have also suggested that prebiotics containing galactooligosaccharides (GOS) can improve adverse effects by increasing iron absorption and protecting against enteropathogens (i.e. *E.* coli pathogenic) by enhancing commensal bacteria.[15,16]

Experimental evidence also suggests that following the current recommendations of taking oral iron two to three times daily may not be the best way to take iron supplements. If daily oral iron supplementation is not tolerated, alternate day dosing of iron can be trialed. Moretti et al. found that high doses of oral iron supplementation (ferrous sulfate 200mg three times daily) increase hepcidin, inhibiting iron absorption for up to 24 hours.[17] When compared to three daily doses, they found that dosing iron 48 hours apart enhances iron absorption as hepcidin levels decrease, removing the mucosal block on iron absorption.[17] This method has been shown to enhance iron absorption and reduce the amount of unabsorbed iron in the GI tract, appearing to be the best way to restore iron levels while minimizing side effects.[5] Further research is needed to determine the long-term effects of iron on the gut microbiome, as well as iron formulations that maximize iron absorption while minimizing side effects[5].

Several alternate forms of iron supplementation are available if oral ferrous sulfate is ineffective or not tolerated. All iron supplementation types should be recommended and monitored by a licensed healthcare provider.

Final Thoughts:

There is still conflicting evidence as to whether the high rates of iron deficiency seen in female athletes are the result of intense physical activity and/or adequate iron intake and further, whether it significantly impairs athletic performance.[1] However, what is known is that dietary modification centered around increasing iron stores should be implemented first, followed by oral iron therapy. As healthcare providers, we can become more aware of iron deficiency and help identify and educate our female athletes who may gain a competitive advantage by balancing their iron stores.

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Leaky Gut and the Competitive Athlete

By Sean Casey, RD, CSCS

AUTHORS BIO:

Sean Casey RD CSCS is a registered dietitian, movement coach and member of the Evolve Wellness Science Team at Hometown Pharmacy of Wisconsin. He specializes in sports nutrition, nutraceuticals, and proactive care.

Quick Hit Summary:

Leaky gut is a condition in which epithelial lining of the intestinal wall breaks down, allowing endotoxins, pro inflammatory cytokines, and other particles to slip from the gut into systemic circulation. Although many recognize stress and diet as a cause of leaky gut, few are familiar with the role of intense exercise in this condition. Intense exercise shunts blood away from the gut leading to local ischemia and intestinal hyperpermeability. Although acute hyperpermeability may be unavoidable, chronic exposure to these conditions may compromise health and performance. Strategies to combat leaky gut in athletes includes consuming nutrient dense foods, optimizing fluid intake during training, stress management techniques such as breathwork and targeted nutraceuticals.

Demands of Competitive Athletics

The demands of being a competitive athlete are something to be respected and admired. The words "*blood, sweat & tears*" are not just a 'rah rah' motivational slogan, but the truth as it relates to the inherent nature of being a competitive athlete.

There are many stresses both seen and unseen that come with the territory. For instance, the physical demands of athletics are easy to appreciate. One can feel their muscles strain under load or exasperated lungs breathe deeply for oxygen.

Mental stresses are front and center as well. Whether competing on a large or small stage, almost all competitive athletes feel a certain amount of pressure to perform well – especially if winning or losing affects their paycheck!

There is a 3rd stress, however, that comes with intense training which often gets overlooked, including by the athletes themselves. That is, the physiological demands placed on the gut. There are two specific challenges to note in this regard:

1) The ability to absorb enough nutrients to fuel athletic endeavors
2) The ability to maintain structural integrity of the intestinal lining vs. developing leaky gut

In this article, we're going to focus on the latter of these two physiological demands placed on the gut while training and competing, highlighting how it occurs as well as ways to offset it through lifestyle intervention.

Leaky Gut – How Does Exercise Induce It?

It's well known that high intensity training shunts blood away from the gut towards the muscles. Specific to endurance training, research indicates that training at 70-80% of VO2max results in a decreased blood flow to the gut leading to local ischemia.[1]

Although short durations of training at 70-80% VO2max probably won't cause much harm, when these intensities are maintained for > 60 minutes, problems can develop.[1] More specifically, cells of the gut responsible for producing mucus, creating tight junction proteins and secreting antimicrobial proteins are damaged.

> It's imperative that sports medicine and physical preparation coaches educate athletes on ways to maintain gut health through food, hydration, nutraceuticals and stress management strategies.

As a result, endotoxins as well as pro-inflammatory cytokines pass through the intestinal epithelial wall and into systemic circulation in a condition known as 'leaky gut'.[1]

During instances when training intensity is even higher, such as seen during VO2max test, leaky gut symptoms may be readily apparent within 20 minutes.[2]

Fans of resistance training are not immune to intestinal hyperpermeability symptoms either. In a study involving 24 college aged students reporting to spend 5-10 hrs /wk exercising, it was found that 6 sets of leg presses between 55-75% one rep max (1RM) led to leaky gut symptoms as evidenced by a rise in intestinal fatty-acid binding protein (I-FABP); a marker of compromised intestinal epithelial integrity.[3]

As it relates to a typical team sport practice, Chantler et al. demonstrated rises in both I-FABP and lactulose:rhamnose ratio (L:R), another marker of leaky gut, following a standardized rugby practice.[4]

Additional Causes of Leaky Gut in Athletes

Other factors, beyond exercise induced intestinal hypoxia, can lead to leaky gut in athletes too.

For instance, many athletes take non-steroidal anti-inflammatory drugs (NSAIDS) to help deal with musculoskeletal pain. Although NSAIDS reduce pain, they also cause collateral damage in the form of impaired structural integrity of the gut lining. This damage is the result of NSAIDS inducing mitochondrial dysfunction, inhibiting enzymes responsible gastric mucus secretion and potentially creating dysbiosis by negatively affecting the gut's natural microflora .[5,6]

Another factor contributing to leaky gut in athletes is mental stress in general. As detailed in the June 2023 issue of *Sports Pharmacy*, heightened levels of stress increase gut permeability. [7]

Last but not least, it appears that eating a diet rich in highly processed foods and low in essential nutrients may contribute to the development of this condition too.[8]

Are we destined to leaky gut if we train hard?!

So far, I've painted a semi gloomy picture with respect to leaky gut and the competitive athlete. However, before the alarmist bells start ringing in your brain, fret not! Intense training won't kill you!

Although transient increases in intestinal permeability may be unavoidable with intense training, athletes can pull on multiple levers to limit its impact and prevent leaky gut from developing into a full-blown issue.

These include:

1) 1) Food
2) 2) Water
3) 3) Nutraceuticals
4) 4) Breathwork & Other Stress Management Techniques

Let's examine each one of these a bit more closely!

Intervention #1 – Food

As aforementioned, one's diet appears to affect the development of leaky gut. Westernized diets, rich in highly processed foods and low in micronutrients contributes to the development of intestinal hyper permeability.[8]

On the opposite end of the spectrum, diets rich in fruits and vegetables can reinforce gut lining through two different mechanisms. First, both fiber and polyphenol antioxidants present within said foods can increase short chain fatty acid (SCFA) production by gut bacteria. SCFA's serve as fuel for the cells lining one's gut and play a key role in intestinal barrier function. Additionally, antioxidants modulate inflammation within the body and increase activity of various antioxidant enzymes. [8] By naturally reducing inflammation through food, less stress is placed on the body as a whole.

From a pragmatic point of view, aiming for > 6-8 servings of fruits and veggies per day, with one serving being approximately size of one's fist, is a good starting place. A note of caution, whole fruits and vegetables consumed within 60 minutes of a training session may upset one's stomach. Thus, timing of fruit and vegetable intake should be taken within consideration.

Intervention #2 – Water

Multiple studies have shown that fluid restriction during exercise leads to increased gut permeability.[9] In one particularly fascinating study completed by Lambert et al, 20 trained endurance runners with a mean age of 22 years old completed three separate 60 min treadmill runs at 70% VO2max under the various conditions:[10]

1) No Fluid
2) Carbohydrate Liquid Solution
3) Plain Water

Upon conclusion of the study, researchers found that when running under the 'no fluid' condition, runners experienced increased gut permeability despite only modest dehydration (1.5% loss of body weight).[10] In contrast, under both conditions when a liquid beverage was consumed, gut integrity was kept in tack as evidenced by no changes in L:R ratio. No differences in gut permeability were observed between the carbohydrate and water only conditions.

These results further underscore the importance of fluid intake while training to not only enhance athletic performance, but to mitigate exercise induced leaky gut.

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Intervention #3 – Nutraceuticals

Various research teams have investigated the use of nutraceuticals to reduce leaky gut symptoms in athletes.

Glutamine has been shown in multiple studies to reduce the normal rise in intestinal hyperpermeability seen with intense exercise.[11-13] In these studies, glutamine intake ranged from as low as 3g per day (combined with 0.69g of cysteine) to as high as 0.4g/lb per day.

Bovine colostrum, which is produced by cows during the first few days of lactation, has also been shown beneficial in combating exercise induced leaky gut. Efficacious doses appear to be 20g/d.[9] Additional nutraceutical agents which may provide benefit include zinc carnosine, probiotics, prebiotics and various polyphenol supplements.[8,9]

Intervention #4 – Stress Management

As aforementioned, one of the biggest contributors to pour gut health is general stress. There are multiple methods to manage stress such as enjoying time in nature, reading, social interaction and various mindfulness/meditation techniques.

One particular stress management strategy that has gained increased media exposure as of late is the use of breathwork. There are various breathing exercises one can employ to manage stress levels including box breathing and cyclic sighing. Box breathing employs equal inhales, exhales and pauses between each segment of a breathing cycle. In contrast, cyclic sighing is characterized by deep breaths followed by relatively longer exhales.

In a fascinating study examining the impact of general mindfulness vs. box breathing vs. cyclic sighing on mood in 108 subjects over the course of 30 days, researchers at the University of Stanford found that cyclic sighing appeared to provide the strongest benefits.[14]

Wrapping Things Up

Intense training is an integral part of any serious athlete's training regime. Although this can spur amazing athletic performance, if not properly managed, it can lead to erosion of one's intestinal lining causing leaky gut. As a result, endotoxins, inflammatory cytokines and other molecules pass from the gut into systemic circulation.

To combat this, it's imperative that sports medicine and physical preparation coaches educate athletes on ways to maintain gut health through food, hydration, nutraceuticals and stress management strategies.

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What to do About Bowel Movements in Athletics

By Dr. Matthew Liaw, Pharm.D.

AUTHOR BIO:

Matthew Liaw is a pharmacist with ten years of service to Navajo people at Crownpoint Healthcare. He is also an amateur distance runner specializing in the 10k, half-marathon, and marathon. As a pharmacist, he has led a medication error subcommittee, run a pain management clinic, and led an antimicrobial stewardship program. The runner in him is a scientist who enjoys repeating physiology trials to see how valid they are for his training. Some of his favorite moments at the UNM physiology lab include testing how shoes affect running economy, testing the impact of an extended interval block, and comparing methods of body fat testing. His dream is to bring his expertise in pharmacy and passion for running together and become a sports pharmacist.

What is Causing These Gut Problems?

Constipation and diarrhea are common concerns to athletes preparing for a competition. The idea of many months of training being derailed because of a simple gut issue is stressful.

Although it is difficult to study the causes of gut issues leading up to competition, current understanding from available research and anecdotes sheds some light on this issue. The problem has typically been broken down into 3 categories. These are physiological, mechanical, and nutritional (Jeukendrup, Gleeson 2019).

Two physiological causes that may cause GI complaints are reduced blood to the digestive system and heightened anxiety. Working muscles demand nutrients and oxygen which are delivered by the circulatory system. In order to increase blood flow to active tissue, blood flow to the digestive system is reduced. Hot conditions also prompt the body to divert blood to the skin which further decreases blood flow to the intestines. In addition, a person can have heightened anxiety leading up to a competition.

Mechanical causes refer to the external impact on the body as a person exercises. Repetitive impact on the intestinal lining is thought to increase flatulence, diarrhea, and urgency. This impact is also thought to cause incidences of occult blood after running events. Another mechanical cause is posture. For example, a runner is upright during exercise while a cyclist in an aero position is horizontal. The runner is expected to experience more lower GI symptoms while the cyclist is expected to suffer more upper GI symptoms.

Nutritional causes is one area an athlete has control over. These causes include dehydration and indigestion of certain nutrients. Nutritional practices have been shown to influence GI complaints during competition. One study done by Rehrer and colleagues on Half-Ironman triathletes found that those who had eaten within 30 minutes of starting, had a high protein pre-race meal, or a high-fat pre-race meal experienced more urgency to vomit or did vomit. The study also found beverage choice and fiber content influence the incidence of GI complaints.

Dealing with Constipation

Medically, constipation is defined as having three or fewer bowel movements per week. Stools are often lumpy and hard and passing stool is very difficult. The most common approach to managing constipation is through diet. Increasing insoluble fiber is recommended to add stool bulk and retain water. This creates a softer and larger stool and decreases stool transit time (Jeukendrup, Gleeson 2019). Foods that contain high amounts of insoluble fiber include whole grains, bran, vegetables, and fruit skins. Increasing soluble fiber is beneficial to maintaining a healthy microbiome which may be beneficial to those constipated. Foods containing these include legumes, oats, fruit, and root vegetables. However, if diet changes are insufficient, an athlete can look to using over-the-counter pharmaceuticals.

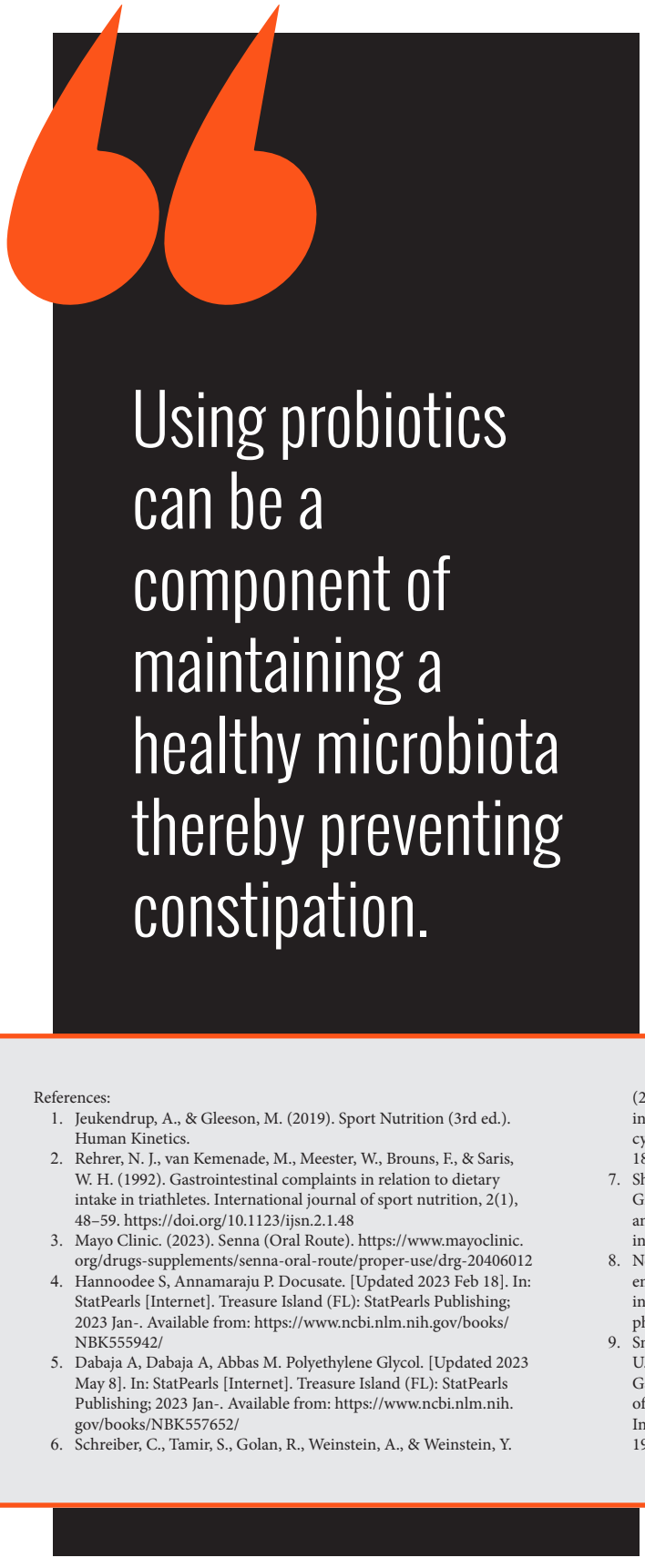
One typically looks at different types of laxatives when managing constipation. A stimulant class drug like senna can be used to create

Athletes will more commonly encounter diarrhea during training and competition. This is characterized by loose, watery stools before or during competition.

bowel movements in six to twelve hours. A stool softener like docusate can be used to prevent constipation and keep bowel movements regular. Polyethylene glycol (PEG) is an osmotic agent that prevents water reabsorption thereby increasing water in the stool. It is typically used in cases when infrequent bowel movements persist for several weeks. In addition to pharmaceuticals, the use of probiotics may help reduce constipation (Schreiber, et al. 2021). For athletes, they should contain a mix of Lactobacillus acidophilus (CUL60), L.acidophilus (CUL21), Bifidobacterium bifidum (CUL20), and Bifidobacterium animalis (CUL34). The use of these agents can relieve constipation. However, an athlete should be cautioned about the risk of diarrhea and intestinal cramping. A proper trial and understanding of how one's gut reacts to such agents is recommended if an athlete plans on using such agents around a competition.

Dealing with Diarrhea

Athletes will more commonly encounter diarrhea during training and competition. This is characterized by loose, watery stools before or during competition. Dietary mistakes that may exacerbate this symptom include consuming lactose, consuming high-osmolarity beverages, consuming too much fiber close to an event, consuming concentrated fructose without glucose, and improper hydration. Because mild lactose intolerance is common, some recommend milk products be avoided within 24 hours of competition (Jeukendrup, Gleeson 2019). The athletes who consumed hypertonic beverages as opposed to iso- or hypotonic beverages also experienced more GI complaints (Rehrer, et al. 1992). In addition, Rehrer and colleagues found that athletes who consumed fiber-rich foods pre-race all had intestinal cramps during competition. Because high osmolarity beverages increase GI symptoms,



many recommend consuming a mixture of carbohydrate substrates instead of fructose or glucose alone. This is because the combination of a mixed carbohydrate solution increases both water and carbohydrate absorption into the bloodstream (Shi et al. 1995). With increased absorption, less water and carbohydrate will transit into the large intestine to cause diarrhea. Finally, dehydration is associated with decreased gastric emptying of fluids (Neufer, Young, and Sawka 1989). This can increase the risk of cramping.

Keeping a Healthy Gut

Approaching constipation and diarrhea management for an athlete is a challenge. It requires the athlete to understand their body and the effects of the environment on it. Using probiotics can be a component of maintaining a healthy microbiota thereby preventing constipation. Its use might be beneficial to replace beneficial bacteria one might lose after diarrhea. Maintaining a journal on how different nutrition strategies affect the body can help create a smoother race day.

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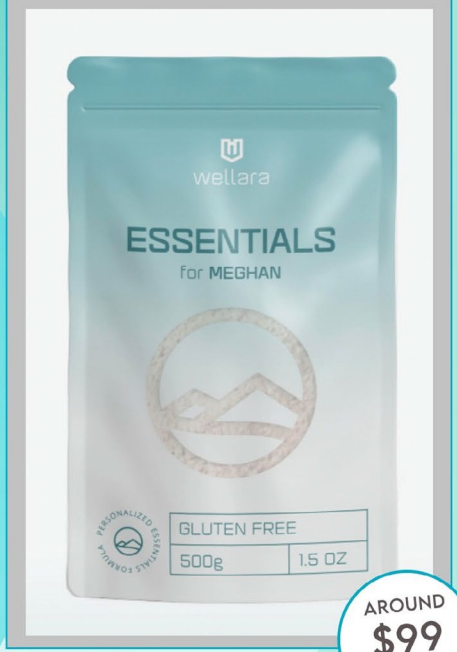

AROUND $99 A MONTH

BLEND OF 42+ ESSENTIAL NUTRIENTS THAT SUPPORT*:

MUSCLE RECOVERY
ENERGY
METABOLISM
FOCUS, COGNITION & STRESS MANAGMENT
SLEEP
IMMUNITY

SAY "NO" TO MORE PILLS

GET THE BEST MEDICINE RIGHT AWAY
FOOD & ESSENTIAL NUTRIENTS!

SHIPS ANYWHERE IN THE USA!

SCAN QR CODE TO GET YOUR OWN CUSTOMIZABLE ESSENTIAL NUTRIENT BLEND & PERSONALIZED MEAL PLAN!

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I am Sorry !!!!

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