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Functional Medicine and Inflammatory Bowel Disease: An Evolving New Approach to IBD Care

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Inflammatory bowel disease is a global disease with incidence and severity rising in Western and industrialized cultures. This increase in autoimmune diseases such as IBD can be influenced by many things: genetics, environment, nutrition, and lifestyle. Functional Medicine is a science-based, personalized approach to healthcare that focuses on understanding the underlying root causes of disease and illness. It seeks to uncover the complex connections between genetics, environmental factors and lifestyle choices contributing to disease manifestation and progression. The principles of Functional Medicine can be utilized to help patients with IBD by making connections between a person and modifiable lifestyle factors. Using a multi-modal functional medicine-based program for IBD, patients can experience improvement in both symptoms and gut inflammation. As the treatment of IBD patients evolves, Functional Medicine can play a significant role in the overall care of the IBD patient resulting in improvement in quality of life and patient outcomes.

INTRODUCTION

In the early 1990s, a group in Victoria, British Columbia, Canada, laid the groundwork for what would become The Institute for Functional Medicine. The goal was to merge traditional medical care with advanced scientific research. This initiative was inspired by the historical concept of functional medicine, dating back to the 19th century. Functional medicine is a holistic, science-based, personalized approach to healthcare that focuses on understanding the underlying causes of disease and illness. It views the body as an interconnected system rather than separate, individual parts. The principles of functional medicine are rooted in lifestyle choices and nutrition with the goal of restoring health and improving overall function. It is not a substitute for conventional medicine,

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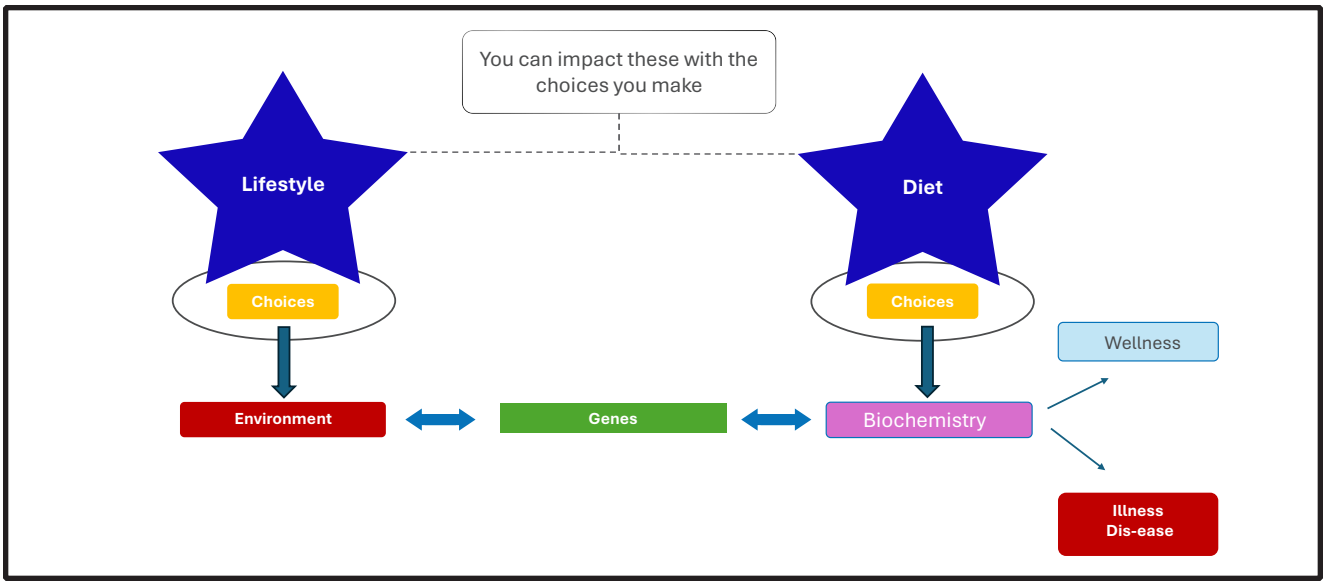


Figure 1. Lifestyle and nutrition influences can affect genetic expression resulting in optimal health or illness/dis-ease.

but the principles can be applied as adjunct care to conventional medicine and serve as a model for the management of chronic, complex diseases. In functional medicine each patient is an n-of-1 and rejects the "one size fits all" concept of care.[12] Functional medicine care aims to improve clinical outcomes and quality of life, create balance and self-discovery, and guide the practice of preventative healthcare.

Inflammatory Bowel Disease (IBD) is an umbrella term that encompasses the diseases Crohn's disease (CD) and ulcerative colitis (UC). It affects millions globally and presents a significant burden to individuals and healthcare systems alike. Traditional treatment modalities have predominantly focused on symptom management through pharmacological interventions. Recently, the use of functional medicine as a transformative approach to IBD management has begun emerging.

Conventional medicine focuses on arriving at a diagnosis and treating symptoms. It is disease-oriented, provider focused, and treatment is symptom-based and disease-specific. Functional medicine practitioners attempt to understand why the disease occurred and notice the linkages between lifestyle, nutrition, mental health, socioeconomic influences, and environmental factors. It treats the body and focuses on root causes while encouraging prevention. In functional medicine, every person has their own origin story.

We live in an era where chronic disease is an epidemic. Roughly 50% of adults have at least one chronic health condition and 25% have 2 or more.[1,2] With the rise in incidence of chronic disease, costs have risen as well. Chronic disease management accounts for 86% of all healthcare costs, and this figure continues to grow.[3] The incidence and prevalence of IBD continues to rise globally in Western and newly industrialized Asian countries.[4] It is becoming quite clear that pharmacologic treatment alone is not enough for this growing epidemic. Our pharmacologic advances in the treatment of IBD over the past 20 years have grown, but the disease is not slowing down. It is unlikely medications alone are going to reverse this trend.

Genetics, the Immune System, and the Environment

The pathogenesis of IBD is best described as an interplay of three domains: genetics (notably, first degree relatives), the innate and adaptive immune system, and environmental exposures. With this in mind, we can further divide these contributors into modifiable and non-modifiable factors. Diet and lifestyle can modify both the risk of developing IBD and overall severity of disease. Lifestyle choices, such as smoking and exercise, contribute

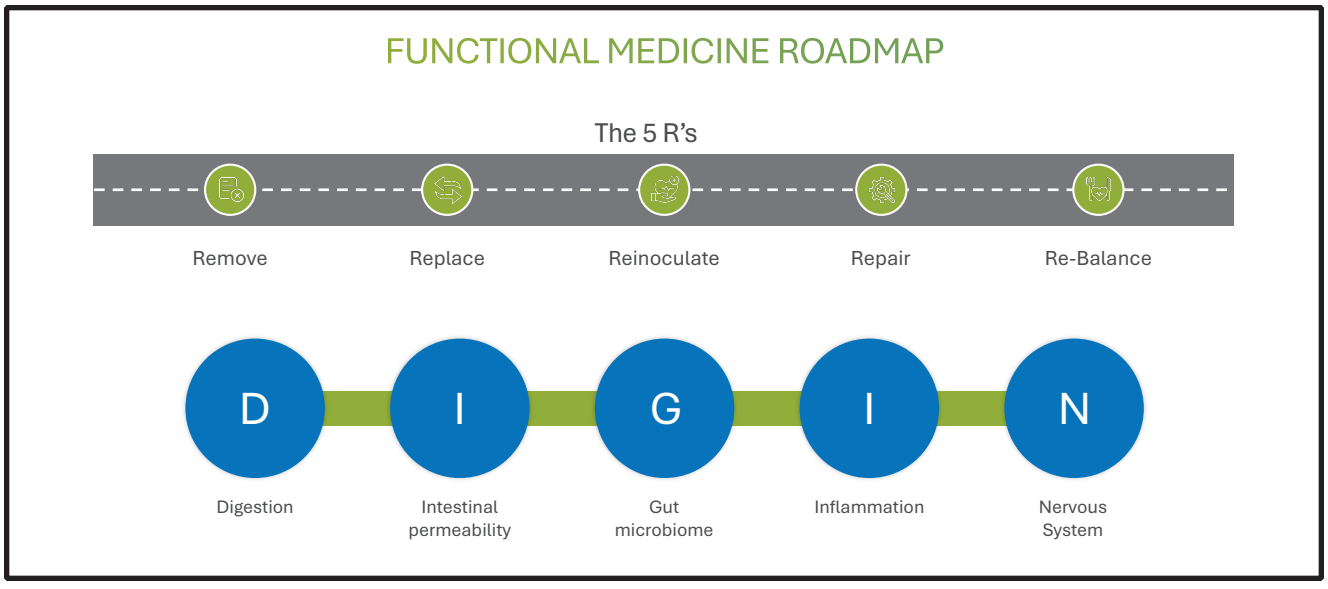


Figure 2. The Functional Medicine Roadmap with the 5 R's and "DIGIN" Framework

to the environment you live in while your diet influences the biochemical makeup and microbiome of the gut. Both factors are the focal points of a functional medicine practitioner's evaluation and management. Functional medicine challenges genetic determinism in that diet, lifestyle, and our environment can determine health outcomes.[1,2]

Disease Modifiers and Environmental Risk Factors

The increase in IBD prevalence may partially be explained by modifiable lifestyle factors. For example, changes in the composition of the gut microbiome can negatively or positively modify the risk for IBD. While certain strains such as *Bifidobacterium* and *Firmicutes* are protective, *Escherichia coli* and *Enterobacteriaceae* are known to increase the risk of IBD. Higher intake of ultra-processed foods such as cheeses, sweets, and pastries are associated with a higher risk of Crohn's disease.[5] Chen et al. showed a nearly 2-fold increase in the risk of CD in patients with higher intake of ultra-processed foods. Patients with pre-existing IBD have also been shown to have higher intake of ultra-processed foods and are four times as likely to have had an IBD-related surgery. Sasson and colleagues expertly described the causation between diet and inflammation.[6] Certain dietary patterns and nutrition status can modify the diversity of the microbiome, increase gut permeability, and alter immune cell dysfunction. All of these contribute to the development and progression of IBD. In a functional medicine model, we think about things in relation to the mnemonic DIGIN: Digestion, Intestinal permeability, Gut microbiome, Inflammation, and Nervous system.

In addition to diet, other environmental triggers such as smoking, antibiotic use in childhood, oral contraceptives, history of appendectomy, and vitamin D deficiency have all been shown to increase the risk of IBD. Conversely, breastfeeding and tea or coffee consumption have been shown to be effective in lowering risk.[4,7] For children with CD, those who had exposure to maternal smoking were at higher risk of hospitalization within the first 3 years of diagnosis. Conversely, children with CD who were breastfed as infants were less likely to progress to structuring or penetrating phenotypes.[8] These are just a few of the many examples of how modifiable lifestyle factors influence the risk and severity of IBD.

The Functional Medicine Roadmap: The 5 R's

Functional medicine focuses on the effects of sleep, exercise, nutrition, stress, and human relationships and their contributions to the overall health of the human body. For IBD, a functional medicine model can promote microbiome diversity resulting in a healthy gut microenvironment. "The 5 R's" is a

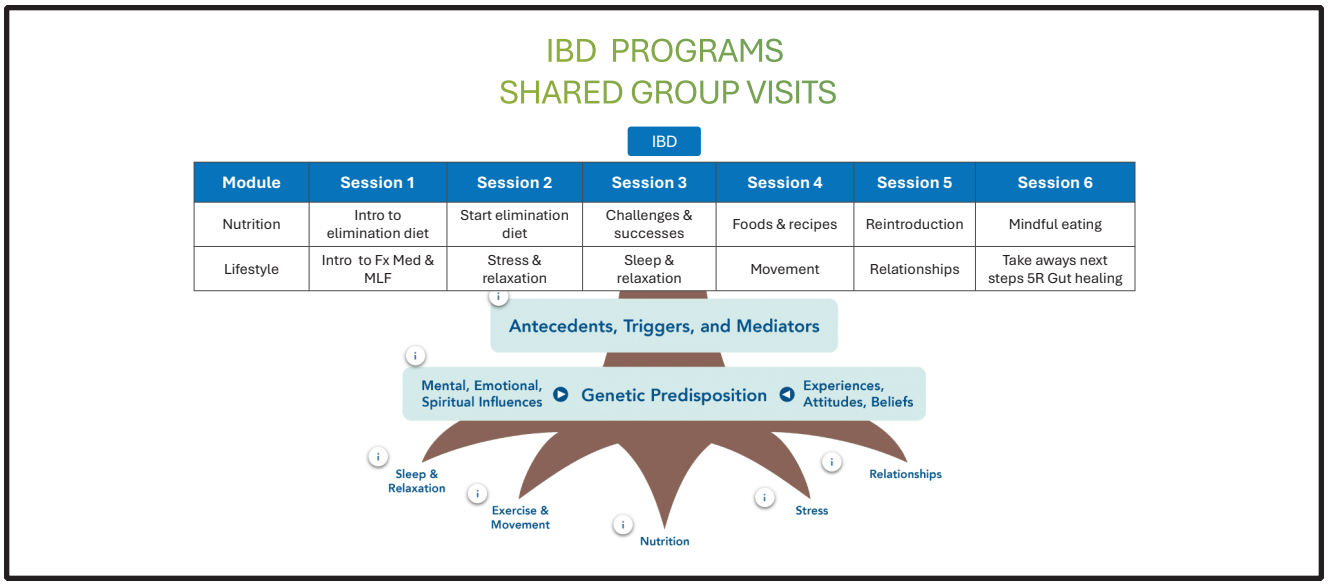


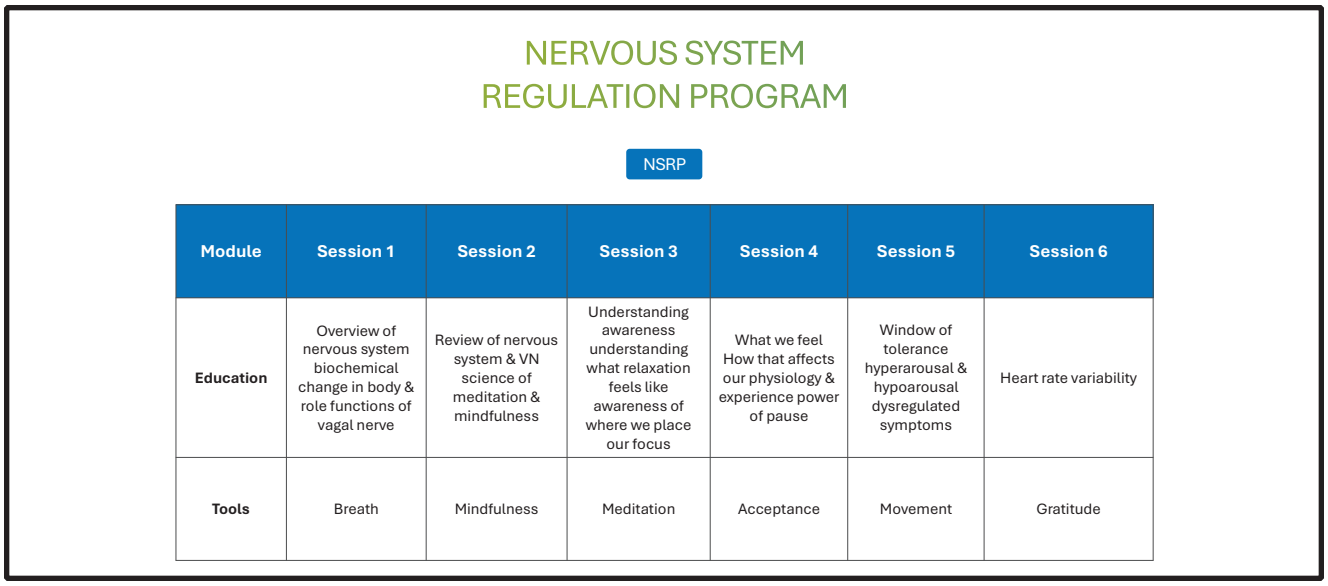
Figure 3. ID Programs: Shared Group Visits

functional medicine framework for gut restoration: Remove, Replace, Re-inoculate, Repair, and Re-balance.

In the REMOVE phase, the goals are to identify and remove dietary triggers, consider any current medications that can trigger dysbiosis or inflammation, and examine other dietary and lifestyle factors that drive dysbiosis. In some patients an elimination diet is helpful to promote body awareness of food, identify food triggers, use phytonutrients to heal the gut and support a healthy microbiome. The elimination diet focuses on common triggers of inflammation including dairy, eggs, gluten, peanuts, shellfish, beef/red meat, soy, corn, refined sugar, coffee/caffeine, and alcohol. Any diet changes or elimination diets should always be supervised by an experienced functional medicine provider or trained dietitian (Figure 2).

In the REPLACE phase, the goals are to support digestion and health by replacing nutrients that are essential to gut healing while focusing on dietary and lifestyle factors that promote wellness. This can be done through nutrients (example: vitamin D, zinc, magnesium, B12), supporting digestion, and focusing on dietary and lifestyle factors that promote health. In the REINOCULATE phase, the focus is to provide care plans to build a healthy microflora and look at the utility of using probiotics, prebiotics, synbiotics (prebiotics + probiotics), post biotics (inanimate microorganisms and their healthy byproducts), and short chain fatty acid as potential tools for care with the goal of supporting disordered intestinal permeability and reversing dysbiosis. It is helpful to remember that one cannot out supplement a bad diet and the "food first" approach should be step one when thinking in terms of how to REINOCULATE the gut.

Diet can either drive dysbiosis or promote a healthy microbiome.[9] In the REPAIR phase, we add back healthy nutrients to support cellular health and prevent inflammation. Vitamin D, L-glutamine, curcumin, botanicals, and immunoglobulins are a few examples that may repair damage from chronic inflammation. Increasing and optimizing phytonutrients are a key component of the REPAIR phase. These nutrients are derived from colorful fruits and vegetables. The aim should be for at least nine servings of phytonutrient-rich foods daily. This is much more than the average American, who gets 2-4 servings daily. Interestingly, each color of food comes with its own benefits in addition to anti-inflammation and vascular health. Eat the rainbow is a term often used in functional medicine. Red and orange foods typically confer anti-bacterial effects while promoting cardiovascular and brain health, prostate health, and cellular protection. Red foods also provide anti-cancer effects. Yellow foods promote digestive, immune, and eye health while supporting anti-inflammatory and protective



Module	Session 1	Session 2	Session 3	Session 4	Session 5	Session 6
Education	Overview of nervous system biochemical change in body & role functions of vagal nerve	Review of nervous system & VN science of meditation & mindfulness	Understanding awareness understanding what relaxation feels like awareness of where we place our focus	What we feel How that affects our physiology & experience power of pause	Window of tolerance hyperarousal & hypoarousal dysregulated symptoms	Heart rate variability
Tools	Breath	Mindfulness	Meditation	Acceptance	Movement	Gratitude

Figure 4. Nervous System Regulation Program

cellular effects. Green foods support metabolic and hormonal health. Blue, purple, and black foods support liver and digestive health. White, tan, and brown foods support immunity, metabolism, and digestion. IBD patients often cannot tolerate a high fiber diet so this goal can be difficult in patients with active disease. Start slow and go slow should be the guidance given to patients with IBD. Be mindful that active inflammation and those IBD patients with strictures need to be on a low fiber diet. Each patient is unique in their inflammatory burden and disease severity, so each dietary plan should also be personalized to them.

If we can recognize that certain foods exert positive influence on overall health on a biochemical level, then such foods can be thought of as medicine. For example, quercetin and vitamin E are known inhibitors of phospholipase A2 – a precursor to arachidonic acid and prostaglandins, which promote inflammation. Quercetin, turmeric, ginger, green tea, and Boswellia are all inhibitors of 5-LOX, a precursor to leukotrienes. Other foods such as garlic, willow, and barberry are COX-2 inhibitors, which downregulates prostaglandin production. All of these are examples of the anti-inflammatory properties of certain foods. Some of these foods have been studied as treatment for IBD. Gut specific turmeric in combination with Qing Dai are examples that have shown promise as a gut-specific treatment for IBD.[13]

The last phase of the 5 R's is REBALANCE, but this should be a focus throughout the IBD care plan from day one. IBD patients are often in a "fight or flight" mode with sympathetic overdrive. Trying to build resilience, reducing stress, and relaxation training should be a focus of care. Some examples of tools to rebalance and support a healthy gut microbiome are mindfulness, stress management, hypnotherapy, heart rate variability tools, and yoga nidra. Engaging in positive lifestyle modifications are the most cost-effective and safe treatments available and are often overlooked in traditional medical care.

Modifiable Lifestyle Factors

How a patient lives is often more important than any time spent with a provider. Chronic disease states often involve multi-system dysfunction. In addition to nutrition, the foundations of health in functional medicine are sleep and relaxation, exercise and movement, stress, and relationships. Data has shown that sleep loss appears to be associated with changes in the microbiota and insomnia can alter the gut microbiome. There are numerous physiologic changes associated with inactivity. Helping patients embrace an active lifestyle will benefit overall wellness. Moreover, stress management can help increase resilience and optimize immune function. Lastly, human relationships play a profound role in human biology. The social threads that connect

us are often more impactful and powerful than the genetic threads.

A real-world example of functional medicine in practice is the Functional Medicine Clinic (FMC) at Vanderbilt University Medical Center. This program utilizes one-on-one and shared group visits to implement the principles of functional medicine. In the one-on-one visits, patients meet with an FMC provider, a wellness coach, and a dietician. During these visits, patients tell their own story of their health and disease. Clinicians elicit key factors predisposing to disease such as their genetic risk and environmental factors, looking for triggering events and mediators or perpetuators of inflammation, such as medication use or past infections. Focusing on modifiable lifestyle behaviors such as sleep, exercise, nutrition, stress, and relationships is the backbone of the program, emphasizing that how a patient lives is vital to their overall health and wellness.

In shared group visits, patients participate in group-based educational sessions every other week over 12-weeks. Each session includes a nutrition and a lifestyle intervention. Topics are described in Figure 3, and all of these are aimed at addressing the root causes of chronic disease. Another program available is a 6-week Nervous System Regulation Program (NSRP). Patients make weekly visits, and sessions are broken down into educational topics followed by an intervention (Figure 4).

The structured FMC program has demonstrated clinical improvement in IBD patient reported outcomes in measures of fatigue, sleep, global symptoms, and IBD-related symptoms.[10] Additionally, a small cohort in the FMC program who had elevated fecal calprotectin levels (a marker of gut-specific inflammation), normalized following completion of the program, with each participant citing motivation to continue the changes they learned from the FM program.[11] In the NSRP, patients have demonstrated improvement in global fatigue and global symptoms.[14]

The benefits of functional medicine may best be described with the following clinical vignette: A woman who was diagnosed with UC after a diarrheal illness and while taking NSAIDs had poor clinical response to conventional mesalamine therapy. Per convention, she was offered escalation to biologic therapy, but she instead expressed willingness to try a functional medicine approach. Listening to her story and timeline, the fundamental issues that stood out were the following: she slept only 5-6 hours per night, was a chronic NSAID user, ate mostly processed foods and drank alcohol weekly. She had limited exercise and a long history of antibiotic use from recurrent UTIs. Additionally, she reported stress from her parents who divorced in high school, and she was bottle-fed as a baby. Upon completion of her personal 5R program, she had marked improvement in symptoms, normalization of a vitamin D deficiency, and normalization of inflammatory markers including fecal calprotectin.

Personalized Treatment Plans

A cornerstone of functional medicine is personalized treatment plans. In other words, it is tailored to the individual's specific health needs and goals. This might include targeted supplementation to address nutrient deficiencies, nutritional changes to support gut health, and natural compounds with anti-inflammatory properties. These personalized interventions are designed to restore balance and functionality to the body and promote long-term remission and improved quality of life for IBD patients.

Functional Medicine and the Future of IBD Care

Functional medicine does not stand in opposition to conventional treatments, but rather complements them. It supports that a portion of health outcomes are influenced by the interaction between genes that are impacted by lifestyle, nutrition, environment, and human relationships. Research has shown thus far that functional medicine can improve outcomes in conditions such as irritable bowel syndrome, inflammatory arthritis, and Hashimoto's thyroiditis. A synergistic approach

that consists of pharmacological treatments and functional medicine strategies can provide the most comprehensive care for IBD patients. It gives patients a more proactive role in the management of their health. This model encourages collaboration between patients and healthcare providers. ■

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