Gastrointestinal Self-Tissue Response Protocol[†]

DEVELOPED IN COLLABORATION WITH OUR SCIENTIFIC AND MEDICAL ADVISORS



In addition to foundational interventions, consider the following underlying factors that can commonly impact self-tissue response in the intestines: cytokine balance, intestinal barrier integrity, microbial balance and immune function.

START HERE

While self-tissue responses in the intestines can be expressed in multiple ways and affect different areas of the digestive tract, the underlying immunology and core approach are the same.

Goals to support self-tissue response will vary depending on whether the patient is experiencing active symptoms. Intervention should begin with focus on rebalancing T-helper cell populations, modulating cytokine activation and promoting neuroimmune health.[†]

Refer to the PureResponse® Self-Tissue Response Protocol for step-by-step guidance.

FOUNDATIONAL SUPPORT

The following protocol recommendations should be considered at Step 3, or week 5, of the <u>PureResponse®Self-Tissue Response Protocol</u> mentioned above.

In addition to a healthy diet and lifestyle, consider the following foundational supplements to support overall health and well-being:

- Pro-Resolve Omega (PRVO6) or O.N.E. Omega (ONO3 / ONO6)
- PureBi•ome™ G.I. (BIOG6)
- Magnesium (glycinate) (MG1 / MG3 / MG9)
- <u>Digestive Enzymes Ultra</u> (DEU1 / DEU9) or
 <u>Digestive Enzymes Ultra</u> with Betaine HCI (DEUB1 / DEUB9)

Some patients may benefit from the addition of Betaine HCl, however, HCl can irritate the gastric mucosa and may be contraindicated in patients with upper Gl symptoms. Use of Betaine HCl is advised only in clinical evidence of inadequate HCl production.

TARGETED NUTRIENTS

Stand-alone nutrients should be considered in addition to foundational support based upon lab results and/or symptoms. Retesting is recommended to determine the need for extended use.

- Vitamin D₃ 25 mcg (1,000 IU) (VD11 / VD12 / VD16)
 Assessment: 25-hydroxyvitamin D
- <u>UltraZin Zinc</u> (UZ9)
 Assessments: Zinc RBC, Copper/Zinc ratio
- OptiFerin-C (OF26)
 Assessments: Serum iron, serum Ferritin, Transferrin
 Saturation, TIBC, UIBC
- Calcium (MCHA) (CH31)
 Assessment: DEXA Scan

- Liposomal Glutathione liquid (LGL)
 Assessment: Whole Blood glutathione
 The administration of supplemental iron can generate free radicals and impact glutathione levels. Blood levels of glutathione should be monitored with the use of supplemental iron.
- PureMelt B₁₂ Folate (PMLB9)
 Assessments: Urinary Methylmalonic acid and Formiminoglutamic acid





TARGETED SUPPORT

The products in this category support common clinical objectives related to self-tissue response in the intestines. Choose from the options listed below:

CLINICAL OBJECTIVE:	ASSESSMENT*	PRODUCT RECOMMENDATIONS	SUGGESTED USE
Healthy Mucosal Immune Response or Abdominal Comfort	Stool testing for microbial balance, short-chain fatty acid production (SCFAs), fecal or serum zonulin or self-reported occasional abdominal discomfort	Epi-Integrity Powder (Order Code: EIP1) Promotes G.I. comfort and broad-spectrum G.I. integrity support by targeting healthy modulation of mucosal immune responses.*	1 scoop, 1-2 times daily in 8 ounces of water or juice
		SunButyrate [™] -TG Liquid (Order Code: BTGL) Supports intestinal barrier health, mucosal barrier function and abdominal comfort. [‡]	1 teaspoon, 1-3 times daily with meals
	Increased immune response in the colon	Curcumin (Order Code: CUR1 / CUR6) Contains Curcumin C3 Complex® to support colon and cellular health.	2 capsules, 1-3 times daily between meals
	Self-reported occasional abdominal discomfort	Boswellia AKBA (Order Code: BWA1 / BWA6) Helps support gastrointestinal health. AKBA may provide gastrointestinal support by maintaining healthy lipid signaling in the epithelial lining of the digestive tract.	1 capsule daily with a meal
Microbiome Support	Dietary assessment for fiber and polyphenol intake or stool microbiome	Poly-Prebiotic powder (Order Code: PPRP1) Polyphenol and prebiotic combination boosts bifidobacteria and microbiome diversity.	1 serving, 1-2 times daily, mixed with a beverage or into food
Detoxification and Antioxidant Support	Dietary assessment for antioxidant intake or whole blood glutathione, GlycA	NAC + Glycine powder (Order Code: NGY1) Promotes antioxidant defenses and the body's natural detoxification process. [‡]	1 scoop daily, mixed with 8 ounces water, between meals





TARGETED SUPPORT CONTINUED

The products in this category support common clinical objectives related to self-tissue response in the intestines. Choose from the options listed below:

Cellular Energy	Self-reported fatigue	B-Complex Plus (Order Code: BCP1 / BCP6) Supports cellular energy production and nutrient metabolism. ⁴	1 capsule, 1-2 times daily with meals
Healthy Stress Response or Mood Support	Self-reported occasional stress	Daily Calm (Order Code: DCM6) Supports relief for occasional anxiety and promotes positive mood. or	1 capsule daily with or between meals 1 capsule daily with or between meals
		Ashwagandha (Order Code: ASH1 / ASH6) Support for occasional stress and overall physical and mental well-being.	

ADDITIONAL CONSIDERATIONS

The products in this category offer alternative or added support for self-tissue responses affecting the intestines. Choose from the options listed below.

CLINICAL OBJECTIVE:	ASSESSMENT*	PRODUCT RECOMMENDATIONS	SUGGESTED USE
Mucosal Barrier Support	Fecal or serum zonulin	I-Glutamine powder (Order Code: LGP) Helps maintain healthy intestinal integrity by enhancing the intestine's protective mucosal lining.	1 scoop mixed with water or juice, 1-3 times daily, between meals
Muscle, joint & tissue health	Self-reported muscle or joint discomfort, including after exercise	Systemic Enzyme Complex (Order Code: SYC1) Supports joint, muscle and cartilage comfort and helps maintain immune mediator activity.	3 capsules, 1-2 times daily, between meals
Microbial Balance	Stool test for microbial balance	MicroDefense w/Oregano (Order Code: MI31 / MI39) Promotes healthy gastrointestinal tract function and microbial balance.	1 capsule, 1-3 times daily, just before a meal, with 8 ounces of water, for 2-3 months
		Saccharomyces boulardii (Order Code: SB6) Promotes healthy gut flora balance.	2 capsules, 1-2 times daily with meals



DIET AND LIFESTYLE RECOMMENDATIONS

Nutrition

Dietary patterns are a significant environmental factor influencing immune responses in the intestines.

The development of self-tissue responses affecting the intestines has been linked to both the Western diet, known to be high in fat and red meat and low in fiber, and the consumption of ultra processed foods, refined sugars and sugar-sweetened beverages.^{1,2} Alternately, a high fiber diet has been demonstrated to reduce the risk of self-tissue responses in the colon by 40%.³

The American Gastroenterological Association (AGA) advises a Mediterranean diet for patients with self-tissue responses affecting the intestines, as it has been consistently found to reduce the rate of active symptoms compared to any other diet.⁴

Components of The Mediterranean Diet:

- Fruits and vegetables
- Complex carbohydrates
- Olive oil
- Moderate consumption of fish
- Lean proteins
- Low intake of added sugars and salt
- Low in ultra processed foods
- High intake of Omega-3 PUFAs

Some patients, especially those who experience narrowing of the intestine may not tolerate fibrous, plant-based foods. Patients are advised to avoid raw foods. Instead, they should cook or steam, and then peel, mash or blend fibrous fruits and vegetables to a soft consistency.

Patients also report other common food triggers, including:5

COMMON FOOD TRIGGERS		
Gluten	Dairy	
Nuts	Whole grains	
Refined sugars	Fried foods	
Spicy foods	Tomatoes	
Alcohol	Caffeine	

In patients with active symptoms, multiple dietary considerations can be implemented on a short-term basis to reduce symptoms and provide bowel rest, including a low fiber diet, a low-FODMAP diet or an elemental diet.

In their 2024 Clinical Practice Update on Diet and Nutritional Therapies, the AGA also outlines when bowel rest with exclusive or partial enteral or parenteral nutrition is recommended.⁵





As patients often report intolerance to many foods, they will commonly restrict food intake to manage symptoms. Medications commonly used by these patients may also cause occasional nausea, abdominal discomfort or vomiting. These factors combined with protein loss, increased nutrient malabsorption and greater metabolism contribute to the risk of multiple nutrient deficiencies.⁶ Common micronutrient deficiencies are iron, vitamins D and B₁₂, folate, zinc, calcium and magnesium.⁷

It is important for the health care practitioner to provide regular screening for malnutrition by assessing signs and symptoms of unintended weight loss, fluid retention, fat and muscle loss, bone loss, fatty acid deficiencies and micronutrient deficiencies. A care plan should be customized to support a patient's individual macro and micronutrient needs.*

Exercise

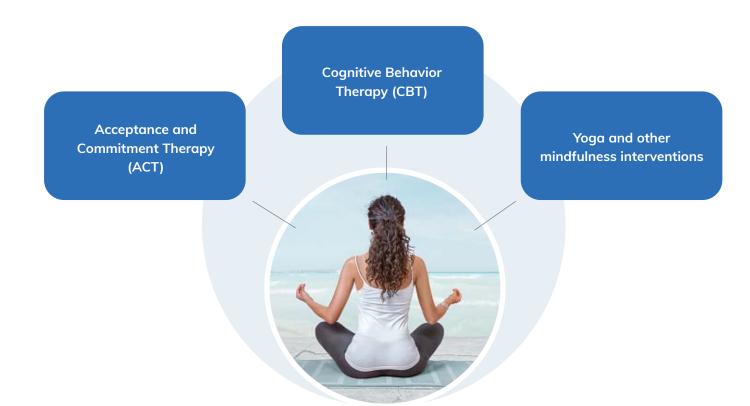
Moderate exercise in patients without active symptoms has been shown to improve both quality of life and bone mineral density and reduce episodes of active symptoms.^{7,8,9}

Stress Management and Mental Health

There is a significant association between low mood and self-tissue responses affecting the intestines.¹⁰

High stress levels can also worsen or activate symptoms, as stress can impact intestinal barrier function, mucin production, microbial balance and immune function.

Cognitive techniques and therapies have been shown to be safe complements to conventional care, with improvements in occasional anxiety and low mood, fatigue, discomfort, symptom severity and health-related quality of life. 11,12,13,14,15,16







ENVIRONMENTAL FACTORS

Certain environmental factors can promote development of self-tissue response in the intestines and impact symptom severity.

Bacterial and Viruses

In addition to altered microbial balance, bacterial and viral agents have been implicated in self-tissue responses in the intestines and worsening of symptoms.¹⁷

Smoking

Encouraging smoking cessation is a vital step in managing patient care, as smoking is known to double the risk of development and symptom severity of self-tissue responses in the intestines.¹⁸

Medications

The use of NSAIDs may increase symptom severity and episodes of active symptoms and has been shown to increase the rate of hospitalizations.¹⁹⁺

ASSOCIATED SUPPORT

Intestinal Health

The relationship between gut microbiota, the immune system, genetic susceptibility and environmental factors is well known in self-tissue responses affecting the intestines.²⁰ Altered balance of the microbiome and mycobiome plays a role in this association.²¹

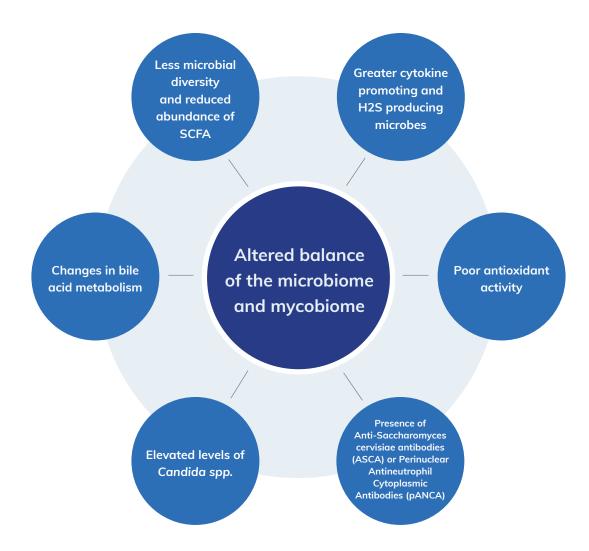
A meta-analysis using glucose and lactulose hydrogen breath tests and 14C-glycocholate breath test, found that approximately 22% of patients with excessive immune activity leading to self-tissue responses in the intestines also have disproportionate and/or abnormal microbiota in the proximal small intestine.²¹ In a later case-control study, the factors associated with this simultaneous occurrence included female gender, low serum total protein, albumin and surgical intervention.²²

The gut microbiome has multiple functions related to health, including regulating intestinal barrier integrity, neurotransmitter and catecholamine production and communication with the central nervous system via the microbiota-gut-brain axis. Alterations in microbial balance or intestinal function can lead to increased intestinal permeability and allow luminal factors to translocate into the bloodstream.²³ Increased intestinal permeability has been associated with self-tissue responses affecting the intestines.²⁴





CHARACTERISTICS OF ALTERED BALANCE OF THE MICROBIOME AND/OR MYCOBIOME



Genetics

Family history is a significant risk factor. Over 100 gene loci have been discovered to be associated with self-tissue responses in the intestines, specifically for encoding of genes involved in maintenance of the epithelial barrier, antigen pattern recognition, autophagy, innate immunological response, coordination of adaptive immune responses and leukocyte recruitment.²⁵

Extraintestinal Concerns

Up to 30% of patients can experience extraintestinal symptoms affecting their liver, kidneys, bones, joints, eyes and skin.²⁶





ADDITIONAL RESOURCES

For additional general recommendations, refer to the following Pure Encapsulations' blog posts and protocols:

GUT HEALTH

- Blog: Nutrient Solutions to Complement the 5R Protocol
- Leaky Gut Protocol‡

Discover how our other clinical tools can enrich your practice:

- <u>Drug-Nutrient Interaction Checker:</u> Provides valuable information on potential interaction between your patients' medications and nutritional supplements.
- <u>PureInsight</u>™: Our healthcare provider support platform helps you deliver personalized diet, exercise, lifestyle and supplement recommendations for your patients.
- Virtual Dispensary: Simplify patient sales and reduce in-office inventory with our Pure Patient Direct virtual dispensary.

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- *Certain medications may be appropriate and should be used under the recommendation of healthcare professional for managing chronic, long-term, and/or serious cases of autoimmunity. Dietary supplements are not intended to replace the use of such medications or treat, cure, or prevent any disease
- +Certain medications may be appropriate and should be used under the recommendation of healthcare professional, including NSAIDs or those used to treat bacterial and viral infections. Dietary supplements are not intended to replace the use of such medications or treat, cure, or prevent any disease.

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