

This protocol was developed with James Greenblatt, MD, a pioneer in the field of integrative medicine for mental health, to help you deliver the most effective care for your patients. In addition to foundational interventions, consider the following underlying factors that can commonly impact mood and emotional well-being: neurotransmitters, cytokine balance, gut health, stress and methylation.

## FOUNDATIONAL SUPPORT

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

- PureGenomics<sup>®</sup> Multivitamin (PGM26)
- <u>O.N.E.</u><sup>™</sup> <u>Omega</u> (ONO6 / ONO3)
- <u>ProbioMood</u> (PBM6)

## TARGETED NUTRIENTS

Stand-alone nutrients should be considered in addition to foundational support based upon lab results and/or assessments. Retesting is recommended with extended use.

- <u>Vitamin D<sub>3</sub> 25 mcg (1,000 IU)</u> (VD11 / VD12 / VD16) Assessment: 25-hydroxyvitamin D
- <u>PureMelt B<sub>12</sub> Folate</u> (PMLB9)
  Assessments: Urinary Methylmalonic acid and Formiminoglutamic acid

<u>Magnesium (glycinate)</u> (MG1 / MG3 / MG9)
 <u>Digestive Enzymes Ultra with Betaine HCI</u> (DEUB9)

- <u>Zinc 30</u> (Z31/Z36) Assessment: Zinc RBC, Copper/Zinc ratio
- <u>B-Complex Plus</u> (BCP1 / BCP6) Assessments: Urinary Methylmalonic acid and Formiminoglutamic acid

# TARGETED SUPPORT

The products in this category support common clinical objectives related to mood.<sup>‡</sup> Choose from the options listed below:

CLINICAL OBJECTIVE <sup>‡</sup>	ASSESSMENT*	PRODUCT RECOMMENDATIONS	SUGGESTED USE
Neurotransmitter Support	Self-reported mood and stress concerns	<b>NeuroPure</b> (Order Code: NOP1) Offers key nutrients to support overall neurotransmitter function, neuronal health and emotional balance <sup>‡</sup>	2 capsules, 1-2 times daily, between meals
		<b>SeroPlus</b> (Order Code: SOP1) Supports serotonin production to promote positive mood <sup>‡</sup>	2 capsules, 1-2 times daily,
		Emotional Wellness (Order Code: EW1 / EW6) Supports emotional and mental well-being and moderates occasional stress‡	1 capsule, 1-3 times daily, between meals

\*This statement has not been evaluated by the Food & Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

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# TARGETED SUPPORT CONTINUED

The following interventions support common clinical objectives related to stress management and relaxation. Choose from the options listed below:<sup>‡</sup>

CLINICAL OBJECTIVE <sup>‡</sup>	ASSESSMENT*	PRODUCT RECOMMENDATIONS	SUGGESTED USE
Neurotransmitter Support	Dietary protein intake	<b>Amino Replete</b> (Order Code: AMR2) Enhances healthy neurotransmitter synthesis with amino acid precursors to support cognitive function and positive mood <sup>‡</sup>	1 scoop daily, mixed with 8 ounces of water or juice, between meals
Cytokine Balance	ESR, CRP	CurcumaSorb Mind (Order Code: MCUM6) Curcumin and polyphenol blend to promote mood, memory and mental sharpness <sup>‡</sup>	2 capsules, 1-2 times daily, with meals
Gut Health	Stool Microbiome	Poly-Prebiotic powder (Order Code: PPRP1) A unique powdered blend of prebiotic fibers and polyphenols to support gastrointestinal, cellular and immune function <sup>‡</sup>	1 serving, 1-2 times daily, mixed with a beverage or into food
Healthy Stress Response or Mood	Self-reported low mood or Mini Mental State Exam (MME)	CogniPhos (Order Code: CGP1) Neuronal support for cognitive performance, mood and behavior‡	2 capsules, 1-2 times daily, with meals
	Self-reported occasional stress	<b>Ashwagandha</b> (Order Code: ASH1 / ASH6) Support for occasional stress and overall physical and mental well-being‡	1 capsule daily, with or between meals

# ADDITIONAL CONSIDERATIONS

The products in this category offer alternative or added support for positive mood. ‡

Choose from the options listed below:

CLINICAL OBJECTIVE <sup>‡</sup>	ASSESSMENT*	PRODUCT RECOMMENDATIONS	SUGGESTED USE
Support neurotransmitter receptor function	Trace mineral hair analysis, Occasional anxiety or irritability	Lithium (orotate) 1 mg (Order Code: L119) Supports emotional wellness, mood and behavior‡ Also available as: Lithium (orotate) 5 mg (Order Code: L19/L11)	1 capsule daily with a meal

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## DIET AND LIFESTYLE RECOMMENDATIONS

Dietary patterns are a significant lifestyle factor for mental health. Food and its components influence not only brain structure and function but also the regulation of gastrointestinal hormones, neurotransmitters and other cellular signals, along with the gut microbiota.

Clinical trials and population studies suggest that traditional dietary patterns, like a Mediterranean-style, whole-food diet, and specific dietary components, including omega-3 polyunsaturated fatty acids (PUFAs), magnesium, vitamins D, B<sub>6</sub> and folate, antioxidants and zinc, may influence for mood concerns.<sup>1</sup>

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## Healthy Dietary Pattern<sup>2</sup>

- Fruits and vegetables
- Wholegrain cereals
- Legumes, nuts and seeds
- Olive oil
- Moderate consumption of fish
- Recommended minimum protein intake of 0.8 g per 2.2 pounds of body weight
- High intake of Omega 3 PUFAs
- Adequate intake of vitamin D, B<sub>6</sub>, folate, zinc and magnesium
- Avoidance of processed foods, refined carbohydrates and sweets

Nutrients from the diet can also alter epigenetic markers, thereby affecting the expression of specific genes associated with mood.<sup>3</sup>

Sleep: Poor quality and quantity of sleep are often symptoms of mood concerns. Conversely, sleep concerns themselves are stressors and increase the risk of changes in mood. Epidemiological studies have shown that 90% of individuals with mood changes related to sadness also have changes in sleep patterns and difficulty with sleep.<sup>4</sup> A relationship exists between low serum levels of **Brain-Derived Neurotrophic Factor** (BDNF) and poor sleep. Individuals with mood concerns have been shown to also have low serum levels of BDNF.<sup>5</sup> Supporting a patient's ability to get 7-9 hours of uninterrupted sleep is a vital component of care.

Exercise: Physical activity is a powerful intervention for mood concerns. Exercises such as walking, jogging, yoga and strength training show greater effectiveness than other types, particularly at higher intensities.<sup>8</sup> Positive effects of exercise have been observed in individuals with and without additional health concerns and for those with varying levels of mood concerns.<sup>8</sup>

FOUNDATIONAL HEALTH **Stress Management:** Mood changes are associated with HPA axis alteration along with altered cortisol and glucocorticoid metabolite patterns.<sup>9,10</sup> Excess cortisol production over prolonged periods can negatively affect mood regulation, sleep, energy levels and the brain's neuroimmune response. Assessing and targeting HPA axis function are key to a patient-centered approach to care.<sup>11</sup>

In addition, stress management approaches like cognitive behavioral programs, meditation and mindfulnessbased strategies can have a positive and significant impact on reducing stress and supporting positive mood.<sup>12</sup>

Light Therapy: Low-intensity blue light or high lux light therapy have both been shown to support a positive mood.<sup>6</sup> Fifteen to thirty minutes of daily morning exposure to sunlight or to 10,000 lux, UV filtered light placed 1-3 feet away, can benefit mood and even augment other care options.<sup>7</sup>

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## ASSOCIATED SUPPORT

### **Gut Health**

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 gut function can lead to increased intestinal permeability and allow luminal factors to translocate into the bloodstream.<sup>13</sup> This can impact neural, hormonal, metabolic and immune pathways, affecting cytokine balance, mood and behavior.<sup>14</sup>

## **Mitochondrial Function**

Oxidative stress, mitochondrial dysfunction and neuro immune responses can contribute to mood concerns.<sup>17</sup> Several categories of pharmaceutical agents, including those used for mood support may also affect mitochondrial function.<sup>18</sup>

## **Cardiometabolic Health**

Altered mood, excess weight, cardiovascular and blood sugar can often coexist and share many of the same biological mechanisms, including changes in cytokine balance.<sup>15</sup> Patients with mood concerns have been shown to have significant variations in different metabolic factors including altered glucose, lipids and albumin profile, as well as abnormal leptin, ghrelin and insulin activity.<sup>20</sup>

#### Genetics

Altered DNA methylation patterns can influence mood changes. Individuals with first degree relatives who have experienced mood concerns have a three-fold risk of also developing mood concerns compared to those without family history of mood concerns.<sup>22</sup> In addition, altered DNA methylation patterns and other gene variants can influence the risk of mood changes and patient response to pharmaceutical agents.<sup>23,24</sup>

Image created with BioRender.com

#### **Immune Factors**

Immune activation and subsequent cytokine release can have a negative impact on mood. Peripherally and centrally circulating cytokines can access the brain and promote changes in monoamine, glutamate and neuropeptide systems, contribute to decreases in growth factors and affect mood and behavior.<sup>15</sup> Individuals with health concerns related to an immune response directed at self-tissue are also at risk of experiencing low mood.<sup>16</sup>

### **Reprodcutive Hormones**

Fluctuations in sex steroid hormones both monthly and throughout the lifespan can make women more vulnerable to mood changes. Women with reproductive system concerns have been shown to have a 2-3 times greater likelihood for changes in mood and mental health.<sup>19</sup>

### **Environmental Toxins**

As a highly metabolic organ rich in fatty tissue, the human brain is especially vulnerable to oxidative damage caused by toxic chemical stress. Exposure to toxins and chemicals in the environment can impact neurodevelopment, neurobehavior, mood and cognitive function.<sup>21</sup>

## Thyroid

Low thyroid function can contribute to low energy and melancholy.<sup>25</sup> Thyroid hormones and their derivatives are highly concentrated in the brain and interact with neurotransmitter receptors, including GABAergic, catecholaminergic, glutamatergic, serotonergic and cholinergic systems.<sup>26</sup>

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## **ADDITIONAL RESOURCES**

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

### **GUT HEALTH**

- Nutrient Solutions to Complement the 5R Protocol (Blog)
- Leaky Gut Protocol<sup>‡</sup>

### **IMMUNE HEALTH**

Immune Defense and Resilience Protocol<sup>‡</sup>

### CARDIOMETABOLIC HEALTH

Cardiometabolic Health Protocol<sup>‡</sup>

### THYROID HEALTH

- Thyroid Health: Looking Beyond TSH and T4 (Blog)
- <u>Thyroid Support Protocol<sup>‡</sup></u>

### MITOCHONDRIAL HEALTH

Mitochondrial Health Protocol<sup>‡</sup>

Discover how our other clinical tools can enrich your practice:

- Drug-Nutrient Interaction Checker: get valuable information on potential interaction between your patients' medications and nutritional supplements.
- PureInsight<sup>™</sup>: 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.

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- \*Genetic testing information is available through PureInsight<sup>™</sup>. Visit <u>PureInsight<sup>™</sup></u> to learn more.
- +Dr. Greenblatt is a retained advisor to Pure Encapsulations.
- The information contained herein is for informational purposes only and does not establish a doctor-patient relationship.

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