Introduction

This guide contains information designed to assist healthcare professionals in their assessment of patients in various stages of physiological stress and to guide in the selection of nutritional supplements for the optimal care of these patients. It is not intended to substitute for the professional’s role in a thorough intake, physical examination, laboratory assessment, diagnosis, treatment, and follow-up of individual patients.

This guide was reviewed by licensed physicians and is for informational purposes only. Opinions and recommendations expressed within are not considered a consensus of medical opinion. While many of the ingredients discussed within have been the subject of controlled clinical trials, others are supported by historical and anecdotal use, preclinical data, or other more preliminary forms of evidence.

Organization by Physiological Stages of Stress
This guide is organized by the three Stages of HPA Axis Resistance that were modeled after the stages of stress adaptation originally described by Dr. Hans Selye in his General Adaptation Syndrome (GAS). Each stage has been interpreted by practitioners and expanded to correlate symptoms with other clinical parameters (e.g., laboratory values) to assist in patient evaluation.

Selecting Products and Dosages
Each Stage comprises a list of “Primary Supplemental Support” ingredients or blends as well as “Additional Considerations.” “Primary Supplemental Support” ingredients or blends form the basis of supporting HPA axis function in that particular stage.

“Additional Considerations” address predisposing or related factors that may be associated with a particular stage, and offer additional or alternate ingredient selections. One or a combination of these ingredients may apply to an individual patient, depending on the healthcare professional’s assessment. If symptoms have been present for a long time, or in more complicated cases, ingredients from the “Additional Considerations” list may be added to the “Primary Supplemental Support” ingredients. As always, supplemental support is enhanced by appropriate lifestyle and dietary changes recommended by a healthcare professional. Use of the Laboratory Parameters and Symptoms checklists will help to identify these factors.
### Stages of HPA Axis Resistance

**STAGE I: HPA ACTIVATION**
- Immediate activation of the nervous system and adrenal gland
- Initiation of the HPA activation, releasing cortisol resulting in the “flight or fight” response
- In turn, the stressor is neutralized through this inflammatory response

**STAGE II: HPA ADAPTATION**
- An adaptation response characterized by hypothalamic release of corticotrophin-releasing hormone (CRF)
- CRF signals the pituitary gland to release adrenocorticotropic hormone (ACTH)
- ACTH stimulates increased cortisol release from the adrenal cortex which in turn quells the inflammatory response
- Once certain cortisol levels are reached, it inhibits CRF and ACTH (negative feedback) and homeostasis returns

**STAGE III: HPA DEPRESSION**
- With repeated exposure to a stressor, thus prolonged cortisol elevation, the hypothalamus and pituitary lose sensitivity – thus the system never turns off, ultimately exhausting the HPA axis
- Left unbalanced, it can have a diverse and irreversible impact on the body

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### Lifestyle and Supplemental Support Considerations

**STAGE I: HPA Activation**

<table>
<thead>
<tr>
<th>Laboratory Parameters</th>
<th>Primary Symptoms</th>
<th>Secondary Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated: Cortisol, DHEA, Blood pressure (sitting to standing), Fasting blood glucose</td>
<td>High stress, Appear high strung, anxious, or agitated, Poor sleep, but little fatigue (‘tired, but wired’), Higher pulse</td>
<td>May suffer acute GI issues (e.g., gas, bloating, constipation, nausea, indigestion, reflux), More likely to be immune compromised</td>
</tr>
<tr>
<td>Within Normal Limits to Low: Serotonin</td>
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</tbody>
</table>

**Stage I Lifestyle Support**

Obtain regular exercise.
Establish regular bed times and obtain sufficient sleep.
Practice relaxation activities (e.g., meditation, yoga, hobbies).
Stop smoking; consider smoking cessation programs.
Avoid or limit alcohol and sugar consumption.
Identify and remove food intolerances
**Stage I Primary Supplemental Support**

**Cortisol-Lowering Herbs:** Ashwagandha (*Withania somnifera*) 200-400 mg; L-Theanine 50-100 mg; Magnolia (*Magnolia officinalis*) 150-300 mg; Epimedium (*Epimedium koreanum*) 75-150 mg; Phosphatidylserine 50-100 mg: take before bedtime.

**Adaptogens:** Rhodiola (*Rhodiola rosea*) 200-400 mg; Ashwagandha (*Withania somifera*) 150-300 mg; Eleuthero (*Eleutherococcus senticosus*) 150-300 mg; Holy Basil (*Ocimum sanctum*) 100-200 mg; Maca (*Lepidium meyenii*) 75-150 mg: take daily on an empty stomach.

**Stage 1 Additional Considerations**

**Lavender Oil:** 80 mg in softgel form daily. Orally administered lavender oil has been shown to reduce anxiety in 4-8 weeks in peer-reviewed, published clinical trials.

**L-Theanine:** 100-300 mg two to three times daily. L-Theanine increases feelings of relaxation, without diminishing daytime alertness.

**Phosphatidylserine (PS):** 200-300 mg daily. PS is a critical component of cell membranes, and it is found in especially high concentrations in the brain and nervous tissues, primarily in the cell membranes of neurons. Supplementation with PS can support cognitive function, reduce stress, and enhance exercise capacity.

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**Stage II: HPA Adaptation**

### LABORATORY PARAMETERS AND SYMPTOMS

<table>
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<tr>
<th>Laboratory Parameters</th>
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<th>Secondary Symptoms</th>
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<tbody>
<tr>
<td>Elevated:</td>
<td>Moderate stress</td>
<td>May be driven and/or over reactive.</td>
</tr>
<tr>
<td>IL-6</td>
<td>Tired</td>
<td>May increase alcohol and tobacco use</td>
</tr>
<tr>
<td>CRP</td>
<td></td>
<td>More likely to have weakened immunity</td>
</tr>
<tr>
<td>Within Normal Limits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortisol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DHEA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serotonin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serotonin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Stage II Lifestyle Support**

See recommendations for Stage I.

**Stage II Primary Supplemental Support**

**Adaptogens:** Rhodiola (*Rhodiola rosea*) 200-400 mg; Ashwagandha (*Withania somifera*) 150-300 mg; Eleuthero (*Eleutherococcus senticosus*) 150-300 mg; Holy Basil (*Ocimum sanctum*) 100-200 mg; Maca (*Lepidium meyenii*) 75-150 mg: take daily on an empty stomach.

**Stage II Additional Considerations**

See additional considerations for Stage I.
Stage III: HPA Depression

LABORATORY PARAMETERS AND SYMPTOMS

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<tr>
<th>Laboratory Parameters</th>
<th>Primary Symptoms</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Low: Cortisol</td>
<td>Fatigued/exhausted</td>
<td>More likely to suffer from pain</td>
</tr>
<tr>
<td>DHEA</td>
<td>Very tired in the evening</td>
<td>May be more prone to allergies</td>
</tr>
<tr>
<td>Serotonin</td>
<td>Poor sleep (difficulty falling asleep and staying asleep)</td>
<td>Less ability to handle stress (even small injuries cause crisis, shaking)</td>
</tr>
<tr>
<td>Blood pressure (sitting to standing)</td>
<td>Low pulse</td>
<td>May report more emotional issues (e.g., anxiety, depression, irritability, frustration)</td>
</tr>
</tbody>
</table>

Stage III Lifestyle Support

Obtain mild to moderate exercise. Practice relaxation activities (e.g., meditation, yoga, hobbies). Eat small, frequent meals to address low blood glucose levels. Increase protein intake. Stop smoking; consider smoking cessation programs. Avoid or limit alcohol consumption.

Stage III Primary Supplemental Support

Adrenal Restoration: Vitamin C 30-60 mg; Thiamine (vitamin B1) 3-6 mg; Riboflavin (vitamin B2) 3.4-6.8 mg; Vitamin B6 6-12 mg; Pantothenic Acid 150-300 mg; Eleuthero (Eleutherococcus senticosus) 150-300 mg; Licorice (Glycyrrhiza glabra) 150-300 mg; Forskolin (from Coleus forskohlii) 10-20 mg: taken daily.

Sleep Restoration: Vitamin B6 (as pyridoxine HCl) 50 mg; Glycine 3 g; Melatonin 3 mg; Water-Dispersible Turmeric (Curcuma longa) Complex 100 mg; L-Theanine 100 mg; L-5-Hydroxytryptophan (5-HTP) 100 mg: take 30 minutes before bedtime.

Stage III Additional Considerations

Adrenal Glandular Extracts: Adrenal cortex extract 150-450 mg and whole adrenal extract 50-150 mg taken with food. Can be used in combination with the Adrenal Restoration recommendations noted above when additional glandular support is necessary.

DHEA (Dehydroepiandrosterone): 5-25 mg daily taken with or without food. Supplemental DHEA restores healthy DHEA levels. Use should be monitored closely. DHEA is not recommended for individuals under the age of 18 years, nor should it be used by pregnant or nursing women. NOTE: exceeding the recommended serving may cause serious adverse health effects. Possible side effects include acne, hair loss, hair growth on the face (in women), aggressiveness, irritability, and increased levels of estrogen.