HPA Stress Profiles – What Are These Tests For?

BioHealth Laboratory offers many test combinations that include the HPA Stress Profile which is the four-point salivary test commonly referred to in the past as the Adrenal Stress Profile. As our knowledge of HPA axis dysfunction advances, we need to shift our paradigm and modify our language to more accurately reflect an integrated understanding of the relationship between the hypothalamus, pituitary, and adrenal glands. When we measure cortisol in a four-point diurnal test, we are not only looking at the health of the adrenal glands, but rather we are assessing the entire system that responds to those stressors which ultimately results in the output of cortisol and DHEA(S) from the adrenal glands. The cortisol and DHEA(S) that we measure are an end-result of a carefully orchestrated stress response involving the HPA axis.

Stress is a part of our daily lives – no one can escape it. How we internalize, manage and respond to stress has a significant effect on health and the development of disease. Stress can undermine our health at its very foundation and leave us predisposed to all disease processes. When we think of stress we often think of major life events such as death of a loved one, divorce, major health issues, etc. While these episodic stressors have consequences, the most common daily stressors are the ones which often go unrecognized and therefore are not adequately addressed. Some of these common modifiable stressors include glycemic dysregulation, poor quality sleep and sleep habits, increased inflammatory signaling and a high level of perceived stress.

The Cortisol Awakening Response (CAR) and Cortisol/DHEA-S data provide us with an assessment of how our patients are managing and internalizing their stress(ors). It allows us to quantify the effects of those stressors on the very system that is responsible for a healthy and adequate response. Measuring cortisol levels within the first hour of awakening provides us with insight into how vital the HPA axis is in responding to stress. Waking up in the morning is like a mini stress test for the HPA axis. If cortisol is excessively elevated, we know the system is revved too high and is in a highly reactive stress response. If the values are low, we know the HPA axis may be weakened due to chronic stress (a downregulation of the system), chronic inflammatory signaling, sleep issues, or disorders like PTSD, chronic fatigue syndrome or seasonal affective disorder. Each of these states would be addressed differently with specific recommendations for the patient’s needs.

The HPA Stress Profile provides us with information regarding how well an individual maintains an adequate cortisol output throughout the day. HPA axis dysfunction can present with several different patterns and it is important to identify these patterns within our patients so that they can be supported adequately. Many of these patterns can be improved by addressing the common modifiable stressors that are so prevalent in our lives and undermine our health on many levels.

Why Is the Cortisol Awakening Response Important?

The Cortisol Awakening Response (CAR) is the predictable rise and fall of cortisol within the first hour of awakening and is essential in evaluating the overall dynamic function of the HPA axis. There are two events that contribute to this dynamic rise in morning cortisol. The first is in response to ACTH output from the pituitary as a part of the normal circadian activities of the HPA axis. The second occurs in response to exposure to daylight with the activation of the suprachiasmatic nucleus in the brain which occurs within 30-45 minutes after awakening and can increase cortisol by 50% from the waking value. These events occur in a timed and metered fashion allowing for a rise and fall of cortisol over a one-hour period.

Running the HPA Stress Profile with CAR allows us to see the momentum of the rising cortisol as stimulated by a healthy HPA axis. Within the first hour of awakening, the cortisol should rise and fall in a predictable manner peaking within 30-40 minutes after waking then showing a predictable decline at the 60-minute mark. The results of the CAR can also help us to more accurately interpret the HPA Stress Profile as the diurnal values may be a direct effect of the cortisol awakening response. Evaluating all of this data gives a much broader picture of what is occurring in the entire system and, more specifically, provides insight into a patient’s internalization of stress which is a major contributor to poor health.

The CAR allows us to determine how robust the HPA axis is and relate those results to an individual’s history. Barring serious adrenal disease, in most cases, the adrenals are able to produce their respective hormones in response to stimulation. It is the...
HPA axis that demonstrates dysfunction in response to stressors when adrenal hormones are low or high. We can measure the response to HPA stimulation by measuring the output of endpoint hormones like cortisol and DHEA-S, however, we cannot assume that the dysfunction resides within the adrenal gland if cortisol or DHEA-S are low or high. Utilizing a Cortisol Awakening Response test, along with Perceived Stress surveys (see below) gives us deeper insight into where the dysfunction is occurring and guides us in developing a prognosis and program for recovery.

Who Should Do This Test?
Maybe the question should be “Who shouldn’t do this test?” The answer would be, “Those without stress on any level.” Chances are, if these people exist, they’re not in your office seeking your help. An HPA Stress Profile with CAR and various add on tests is going to be appropriate for most of your patients and provides an easy assessment of their ability to deal with stressors and is also reflective of how well they have dealt with stressors in the past. An HPA Stress Profile serves as an effective starting point for addressing diet, lifestyle, stress management, sleep and inflammatory triggers that are impediments to getting well. The numbers can say a lot and provides your patients with a quantitative assessment of how they are doing on a foundational level. It has not always been easy to measure a person’s management of stress perception and how it affects their health, but now it is.

What Do These Tests Measure?
Each of these salivary tests measures 4-6 cortisol samples and a molar ratio of DHEA-S. The DHEA-S is measured in the morning sample when it is highest. The DHEA-S is presented in the same units of measurement (molar ratio) as the cortisol so that we can assess a true ratio between cortisol and DHEA-S. We offer tests that evaluate various combinations of the diurnal output of cortisol, cortisol awakening response (CAR), sex hormones and secretory IgA. There are several combinations listed below. For a more complete explanation of sex hormones and secretory IgA, please refer to the test guides for the Female Hormone Profile #209 and Secretory IgA #310.

Basic HPA Stress Profiles –
• #201A HPA Stress Profile - Cortisol X 4, DHEA-S
• #201AC HPA Stress Profile with Insomnia Sample - Cortisol X 5 with optional waking sample, DHEA-S
• #204A Cortisol Diurnal Rhythm - Cortisol X 4 (applicable for pre-adolescents)
• #205A HPA Stress Profile +5 - Cortisol X 4, DHEA-S, Estradiol, Estriol, Progesterone, Testosterone, Melatonin
• #205AE HPA Stress Profile +6 - Cortisol X 4, DHEA-S, Estradiol, Estriol, Estrone, Progesterone, Testosterone, Melatonin

HPA Stress Profiles with Cortisol Awakening Response (CAR) –
• #201-CAR - HPA Stress Profile with CAR – Cortisol X 6, DHEA-S
• #205-CAR - HPA Stress Profile with CAR +5 – Cortisol X 6, DHEA-S, Estradiol, Estriol, Progesterone, Testosterone, Melatonin
• #205E-CAR - HPA Stress Profile with CAR +6 – Cortisol X 6, DHEA-S, Estradiol, Estriol, Estrone, Progesterone, Testosterone, Melatonin

HPA Stress Profiles with Secretory IgA (SIgA) –
• #201A-S – HPA Stress Profile with SIgA – Cortisol X 4, DHEA-S, Secretory IgA
• #205A-S – HPA Stress Profile +5 with SIgA – Cortisol X 4, DHEA-S, Estradiol, Estriol, Progesterone, Progesterone, Testosterone, Melatonin, Secretory IgA
• #205AE-S – HPA Stress Profile +6 with SIgA – Cortisol X 4, DHEA-S, Estradiol, Estriol, Estrone, Progesterone, Testosterone, Melatonin, Secretory IgA

HPA Stress Profiles with CAR and SIgA –
• #201-S-CAR – HPA Stress Profile with CAR and SIgA – Cortisol X 6, DHEA-S, Secretory IgA
• #205-S-CAR – HPA Stress Profile +5 with CAR and SIgA – Cortisol X 6, DHEA-S, Estradiol, Estriol, Progesterone, Testosterone, Melatonin, Secretory IgA
• #205E-S-CAR – HPA Stress Profile +6 with CAR and SIgA – Cortisol X 6, DHEA-S, Estradiol, Estriol, Estrone, Progesterone, Testosterone, Melatonin, Secretory IgA

How Is the Test Performed?
Saliva samples are collected at designated times throughout the day documenting a cortisol rhythm during the waking hours. The first sample for the HPA Stress Profile should be taken 30 minutes after waking – this represents the peak of morning cortisol production. Sex hormones, DHEA-S and secretory IgA measurements are taken from morning saliva samples. A melatonin level is measured in the night time saliva sample.

The Cortisol Awakening Response (CAR) is measured in three saliva samples - #1 upon waking, before getting out of bed, #2 thirty minutes after waking and out of bed, and #3 is sixty minutes after waking. When a test includes the CAR, there will be a total of six cortisol measurements where the first three samples will mark the cortisol levels between 12-1pm, 4-5 pm, and 10pm-12am.

Saliva collections should be done as per the instructions within the test kit. Avoidance of steroidal hormones prior to collecting samples is necessary to avoid contamination of the sample or falsely alter test results. Use of any kind of steroid should be avoided minimally three days prior to collections. Longer
avoidance time may be needed depending on medication, length of use and mode of delivery. This includes oral, topical, inhalant and sublingual forms of medication.

It is recommended to avoid exercise on the day of saliva collections to avoid a rise in cortisol that occurs within 30 minutes after exercise is completed. Elevations in cortisol due to exercise are not reflective of basal HPA axis function. Samples should be taken on a typical work day. Avoid testing on the weekends or days when there is an excessive amount of stress. If an excessively stressful event occurs, vials can be rinsed out and the test can be completed on another day.

Patients should wake at their usual time on the day of testing. Patients who have more access to natural light upon waking will have a higher CAR. The patient should make note of the amount of light exposure so that it can be duplicated for follow-up testing. Patients who do shift work and are working into the night should start collecting samples at their normal wake-up time and adjust the timing of the subsequent collections accordingly.

**From 3 Stages to Patterns of HPA Dysfunction**

The staging of adrenal fatigue provides a simplistic view of the progression of the effects of stress on the adrenal glands. The staging does not consider the underlying mechanisms that contribute to the progression of these stages. In the three-stage model, stress results in an over-production of cortisol due to the increased stimulation by ACTH. As the stressors become chronic, there is an eventual progression to a down-regulation of ACTH production resulting in low cortisol production and low DHEA-S. These stages are often used to determine the level of treatment needed to support the adrenals but they reveal nothing about the origin of the dysfunction.

The progression of these stages and the resulting low cortisol and DHEA-S is likely due to a down-regulation of the HPA axis over time. It may also be due to elevated Cortisol Binding Globulin (CBG) leaving salivary cortisol low and total cortisol as measured in the serum normal or elevated. This is considered a normal adaptation response to repeated bouts of elevated cortisol designed to reduce the effects of cortisol on tissue. As HPA dysfunction progresses, there is a strong down-regulation in the HPA axis due to years of stress-induced metabolic dysfunction. Recovery from this level of HPA axis dysfunction can require years of support, lifestyle modification, stress management, glycemic control and support of the circadian rhythm.

To understand the origin of HPA axis dysfunction, regardless of the “stage,” clinicians should rely upon their history-taking and diagnostic skills in addition to laboratory results. The numbers don’t have much value in diagnosing the patient’s true issues unless those values are put into the clinical history of the patient with attention to the individual stressors that each patient experiences.

In understanding how these values relate to the history of the patient, we can see a variety of patterns emerge when examining the results of HPA Stress Profiles. Read the article *Stages to Patterns - Science-Based HPA Axis Assessment.*

### CAR, Cortisol and DHEA-S Levels – Looking at the Whole Picture

New to the world of HPA axis evaluation is the **Cortisol Awakening Response (CAR)** test. This component of HPA axis evaluation provides a crucial bit of information and deepens our understanding of the results of a 4-point diurnal HPA Stress Profile. An elevated CAR reveals a high level of anticipated stress, melancholic depression or sleep issues. A depressed CAR is commonly associated with chronic fatigue syndrome, PTSD, long-term stress, burnout, seasonal affective disorder and adrenal insufficiency. Please see the extensive list below.

The amount of cortisol produced in a 24-hour period is a dynamic process responding to fluctuating input and output within the HPA axis. The pattern of cortisol output reveals as much information about the patient as does the quantity of cortisol output. The ratio of cortisol to DHEA-S is generally considered to be a measure of catabolic vs. anabolic activities. DHEA(S) not only acts as an anabolic hormone but also opposes the catabolic effects of cortisol.

Optimal health and an overall feeling of wellness result when all of these components are within the normal range. Changing these values through direct supplementation may change the numbers on the test, however, long-lasting benefits can only be attained by addressing dietary and lifestyle issues that support long-lasting change.

### Conditions Related to HPA Axis Dysfunction

**Increased Activity of the HPA Axis**

- Cushing's Syndrome
- Chronic Stress
- Melancholic Depression
- Anorexia Nervosa
- OCD
- Panic Disorder
- Excessive Exercise
- Alcoholism
- Alcohol and Narcotic Withdrawal
- Diabetes Mellitus
- Central Obesity
- Childhood PTSD
- Hyperthyroidism
- Pregnancy
**Decreased Activity of the HPA Axis**

- Adrenal Insufficiency
- Atypical/Seasonal Depression
- Chronic Fatigue Syndrome
- Fibromyalgia
- PMS
- Menopausal Depression
- Nicotine Withdrawal
- Following cessation of glucocorticoid therapy
- Following Chronic Stress
- Postpartum Period
- Adult PTSD
- Hypothyroidism
- Rheumatoid Arthritis
- Asthma, Eczema, Allergies

**Interpretation of Test Results**

A discussion of CAR and HPA Stress Profile results will be included here. For more information on sex hormones and secretory IgA, please refer to the Test Guides for the Female Hormone Profile #209 and Secretory IgA #310. We know that the HPA axis effects the gonadal output of sex hormones which is why a combined panel can be very useful in assessing the relationship between the HPA axis and sex hormones. Including secretory IgA allows us to see the effect of stress on the mucosal immune system – our first line of defense against infections. Seeing this relationship allows us a broader view of the effects of stress on our health.

**CAR Reference Ranges**

<table>
<thead>
<tr>
<th>Time</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waking</td>
<td>8-18 nmol/mL*</td>
</tr>
<tr>
<td>Waking +30</td>
<td>13-24 nmol/mL</td>
</tr>
<tr>
<td>Waking +60</td>
<td>8-24 nmol/mL*</td>
</tr>
</tbody>
</table>

The change between the waking value and the waking +30 value should be 35-60%*.

The change between the waking +value and the waking +60 value should be <33%*.

* These are lab developed guidelines based on peer-reviewed research in published literature.

**What Does an Elevated CAR Mean?**

If the CAR is elevated, the patient may have a high perceived state of stress as well as other stressful drivers both mental and physiological. The HPA axis is in a heightened state of response with high ACTH stimulating release of cortisol from the adrenals. If mental or emotional stress is causing this it’s key to zone on the reasons for this stress and help design appropriate therapies to ease or eliminate the burden.

**What Does a Suppressed CAR Mean?**

If the CAR is suppressed, the patient is experiencing chronic stress and burnout and the HPA axis is down-regulated to protect the system from an overabundance of cortisol. Common causes are sleep apnea, PTSD, seasonal affective disorder, chronic fatigue, and true adrenal insufficiency.

**What Does a Normal CAR Mean?**

A normal CAR indicates that the HPA axis is healthy and responds appropriately to stress. A normal CAR may occur along with an irregular diurnal cortisol rhythm. If the day’s remaining cortisol values are not within the reference range, this reveals the dysregulation of the stress response throughout the day. A healthy CAR reveals that the HPA axis is functional and healthy which makes returning the diurnal values to normal is more easily corrected with nutritional support, lifestyle modifications, glycemic control and 7-9 hours of quality sleep per night.

<table>
<thead>
<tr>
<th>Time</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waking +30</td>
<td>13-24 nmol/mL</td>
</tr>
<tr>
<td>12-1 pm</td>
<td>5-8 nmol/mL</td>
</tr>
<tr>
<td>4-5 pm</td>
<td>4-7 nmol/mL</td>
</tr>
<tr>
<td>10 pm-12 am</td>
<td>1-3 nmol/mL</td>
</tr>
<tr>
<td>DHEA-S</td>
<td>2.0-10.0 nmol/mL</td>
</tr>
<tr>
<td>Cortisol:DHEA-S Ratio</td>
<td>4.0-6.0: 1 molar ratio</td>
</tr>
</tbody>
</table>

**What Do Elevated Cortisol Values on the Diurnal Time Points Mean?**

One or more cortisol values may be elevated on the HPA Stress Profile. If all the cortisol values are elevated, we know that this patient is in an acute state of stress and the HPA axis is responding by driving cortisol up. Evaluate the stress level of the patient in terms of mental/emotional issues, glycemic control, causes of inflammation, exercise, etc. If values are greatly elevated, it is important to ask the patient about steroid use in any form as this can drive values up greatly. If the patient is not using steroids in any form and cortisol values are greatly elevated without a diurnal rhythm, they may need to be evaluated for Cushing’s Syndrome. As a clinician, you should know and understand the symptoms of Cushing’s and refer for further evaluation when necessary.

If single cortisol levels are elevated, this is likely due to stressful events that trigger the HPA axis at certain points during the day. A heightened perception of stress, glycemic dysregulation, inflammatory conditions and poor sleep can contribute to elevated cortisol values. Understanding your patient’s history and their sources of stress will help determine the cause of the elevated cortisol which ultimately helps direct
the appropriate treatment or lifestyle modification.

- What Do Low Cortisol Values on the Diurnal Time Points Mean?

One or more cortisol values may be low on the HPA Stress Profile. If all the cortisol values are low, this patient has been experiencing chronic stress causing the HPA axis to down-regulate to reduce the long-term effect of too much cortisol. If single cortisol levels are low, this too may be a down-regulation of the HPA axis due to chronic stress. Understanding your patient’s history and the cause and duration of their symptoms will help determine the appropriate course of treatment. Assess the patient for glycemic dysregulation, implement the Perceived Stress Screen to determine their perception of stress and rule out infections and other promoters of inflammation.

- What Do High or Low DHEA-S Values on the HPA Stress Profile Mean?

The same factors that affect the production of cortisol also affect the production of DHEA-S as it appears to be under the regulation of the HPA axis and follows the pulsatile activity of ACTH. DHEA-S is produced primarily in the zona reticularis of the adrenal glands but is also produced in the gonads and the brain. DHEA-S is the most abundant steroidal hormone and serves as a precursor to estrogen and testosterone. DHEA-S is an anabolic hormone and opposes and moderates the effect of cortisol.

A high DHEA-S value may indicate that the patient is under acute stress and is triggering the HPA axis. A higher level of DHEA-S is more common in men and women in their late teens and early 20’s as hormones are peaking.

A low DHEA-S value indicates that the HPA axis is down-regulating to reduce the stress response. DHEA-S tends to decrease naturally with age so this is also a factor to consider. Stress may have a more detrimental effect as we age if we cannot produce enough DHEA-S to oppose the effects of cortisol.

- What Is the Significance of the Cortisol:DHEA-S Ratio?

Including the cortisol:DHEA-S ratio helps to refine our assessment of where the patient is in terms of HPA axis dysfunction. The cortisol:DHEA-S ratio are molar equivalents and therefore assessed by the same units of measurement where morning values of cortisol and DHEA-S are compared. A high cortisol:DHEA-S ratio reveals a higher degree of HPA axis dysfunction where the patient does not have enough DHEA-S to down-regulate the catabolic cellular effects of cortisol. In short, tissue breakdown is occurring faster than it is building up. The net effect is a catabolic state.

If the cortisol:DHEA-S ratio is low, the relative amount of DHEA-S is higher. This scenario is usually seen in younger patients with a strong output of DHEA-S that may be coming from gonadal production. In patients who are beyond the age of peak hormone production, a low cortisol:DHEA-S ratio may be due to supplementation with DHEA or other androgens.

Discussion of Treatment Options

Addressing the Four Major Categories of Modifiable Stressors that Cause HPA Axis Dysfunction - There are four major categories of modifiable stressors that contribute to HPA axis dysfunction. The fact that these categories are modifiable gives both clinician and patient the power to make significant changes resulting in health benefits that reach far beyond the HPA axis.

1. Perceived Stress

There are certain events that are inherently stressful and would trigger a stress response in anyone. However, on a daily basis, the HPA axis is triggered by events that are perceived to be stressful or threatening by the individual. The magnitude of the stress response can be provoked by four key factors: 1) novelty of the event, 2) the unpredictable nature of the event, 3) perceived threat to physical body or ego, and 4) a sense of loss of control. Individual characteristics, personality and predisposition largely determine how one will respond when presented with a stressful situation. One of the most useful ways to assess one’s level of perceived stress is through stress questionnaires revealing how subjects feel about the control in their lives.

Perceived Stress Scale (PSS) – This ten question stress survey identifies and quantifies areas of perceived stress in a person’s life. The questions are mainly focused on how the subjects feel about the control in their lives over the past month. This survey combined with a CAR test can give the clinician a valuable overview of a patient’s level of perceived stress and how it is affecting the HPA axis. With this information, the clinician can then help their patients understand how mental and emotional factors are contributing to their quality of health. This is a key component of any effective treatment program addressing HPA axis dysfunction. Read article The Perceived Stress Scale and HPA Assessment.

Mental/Emotional Aspects - Providing patients with a Perceived Stress Scale gives them the opportunity to quantify their level of perceived stress and identify what areas of their lives cause them the most stress. Very often we know that we are stressed but have not taken the time to really identify the most stressful aspects of our lives. We can’t address a problem if we can’t identify it. Encouraging our patients to identify key sources of stress and helping them to devise a plan to either relieve or reframe those stressors can reduce their level of perceived stress. Whether these stressors are related to work, health, finances or relationships, directing our patients to the help they need will give them a sense of control which can greatly reduce the level of perceived stress in their lives.
Neurotransmitter Imbalances – Developing an awareness of our stressors and how we react is a first major step, however, those reactions are mediated by neurochemical signals before they trigger the HPA axis. Nutritional deficiencies, chronic gut inflammation and neurotransmitter imbalances can make it difficult to modify our response to stressful events. Assessing patients for deficiencies and imbalances in this area can further help them to manage and modify their stress response.

Treatment Options:

Adaptogenic Herbs – These can be found in combination formulas or as single herb products. Some are formulated with additional nutrients to support the HPA axis. Adaptogenic herbs help to moderate and turn down the volume on the stress response. Look for products that contain: Ashwaganda, Holy Basil, Rhodiola, Cordyceps, Codonopsis, Schizandra, Siberian Ginseng, Panax Ginseng, Licorice Root Extract (low cortisol, non-hypertensive).

Nutrient Support – Responding to stressors requires a high potency B-Complex, Vitamin C, magnesium, zinc and other trace minerals. Nutritional products that are created especially for adrenal support will provide a good combination of the recommended nutrients.

Neurotransmitter Support – Neurotransmitter testing can help to identify specific deficiencies and might be appropriate if patients do not respond to a well-chosen neurotransmitter support program. For patients with a high level of stress or anxiety, consider: GABA, L-Theanine and L-Tyrosine. If depression exists, consider: 5-HTP to support serotonin production.

Neurosteroid Support – Neurosteroids are endogenous or exogenous steroids that alter neuronal excitability. They are potent modulators of GABA receptors and can modulate feelings of depression and anxiety. Both DHEA and pregnenolone are neurosteroids and can be produced in the brain as well as enter the brain from general circulation as both can cross the blood brain barrier. Both DHEA and Pregnenolone can be taken as drops, capsules or tablets.

2. Sleep

The circadian rhythm directs the physical, mental and behavioral changes that occur within a 24-hour period in response to the cycles of light and dark. Our circadian rhythm is a powerful regulator of nearly every metabolic function in the body. The quality and quantity of sleep that we get each night has a profound effect on our health by synchronizing signals that control our circadian rhythm. Disruption of the circadian rhythm results in HPA axis dysfunction as the timing of metabolic, hormonal and neurochemical events is interrupted.

Sleep is the greatest reset button for the HPA axis and one of the most important ways to rebuild our metabolic reserve. Staying up too late, consuming too much caffeine, getting too few hours of sleep, shift work and traveling across time zones are all factors that disrupt the circadian rhythm. Chronic inflammation can also disrupt sleep as it causes cortisol to rise which can lead to insomnia. Providing sleep support and lifestyle modification tips to promote a better night’s sleep are some of the best ways to restore healthy function to the HPA axis.

Treatment Options

Adaptogenic Herbs – Adaptogenic herbs will help to moderate the stress response and reduce the output of cortisol.

Reducing Inflammation – Inflammation drives up cortisol levels which can make promote insomnia. Determining causes of inflammation and treating appropriately can decrease cortisol allowing for a better night’s sleep.

Melatonin – If melatonin has been measured and is determined to be low, providing a low dose of melatonin may be warranted. Some people can be sensitive to melatonin so starting with 1 mg within an hour of bedtime is best. Supplementing with 5-HTP can also be supportive of melatonin production.

Calming Herbs – Sleep promoting herbs in the form of teas or capsules can help patients to relax and fall into a deeper sleep. Consider formulas containing: Valerian, Passion Flower, Kava Kava, Chamomile, Hops, Lemon Balm.

Phosphatidyl Serine – This can be taken as a supplement to reduce cortisol levels if they are shown to be elevated, particularly at night.

Epsom Salt Baths – Epsom salts contain magnesium sulfate which is absorbed through the skin while soaking in an Epsom salt bath. Magnesium can aid the body in relaxation and is crucial for many biochemical processes. The sulfate portion of the molecule serves as a source of sulfur which is a key nutrient in detoxification.

3. Glycemic Dysregulation

The stress response is designed to release energy stores making them available to support our physiological...
need to respond to a stressful situation. Cortisol is a glucocorticoid and is fundamental in the regulation of glucose metabolism. If cortisol is elevated in a stress response, glucose stores are mobilized to be used as energy. The presence of glucose in the blood increases insulin production allowing for the glucose to enter the cells where it can support metabolic processes. Most of our daily stressors that result in an increased cortisol production do not require an infusion of glucose to support our ability to “fight or flee.”

In our current culture of stress, fighting or fleeing would likely be an inappropriate response to most of the stressors that we experience today. Since we can’t use all of the glucose that was mobilized to support that stress response, it gets stored as visceral fat. We are left with a condition that increases stress inducing inflammatory mediators which further promotes release of cortisol.

Glucose is the primary fuel for the brain and the hypothalamus is particularly sensitive to falling glucose levels. Hypoglycemia is a potent trigger of the HPA axis as an effort to increase cortisol and restore adequate glucose levels in the blood. Diets high in carbohydrates and sugar often result in hyperglycemia and hyperinsulinemia where glucose is stored as visceral fat as an effort to return blood glucose levels to the normal range. As stated above, increased visceral fat results in inflammatory mediators further promoting release of cortisol. Glycemic dysregulation results in a vicious cycle of elevated cortisol and metabolic dysregulation.

**Treatment Options**

**Dietary Modifications** – Reducing fluctuations in blood sugar reduces stress on the HPA axis. Maintaining a diet that consists mostly of low glycemic foods is key. An abundance of raw and cooked vegetables, low sugar fruits, a modest amount of whole grains, quality protein and healthy fats consumed in regular meals throughout the day will support a stable blood glucose level. Reducing refined sugars and carbohydrates while getting adequate soluble, insoluble and fermentable fibers can help to make great strides towards weight loss and glucose management. The Mediterranean diet, modified Paleo diets, The Rosedale Diet, etc would all be good options.

**Nutrient Support** – Supplement formulations containing chromium picolinate, vanadium, Bitter Melon, Cinnamon extract, Gymnema Sylvestre and alpha lipoic acid can help to stabilize fluctuating glucose levels.

**Exercise** – Regular exercise 4-6 times per week stabilizes glucose and insulin levels. Consistency is more important than intensity, however, and participating in new forms of exercise keeps the body challenged in a variety of ways while staving off boredom and promoting enthusiasm.

### 4. Inflammatory Signaling

Cortisol is a powerful anti-inflammatory steroid. Inflammation anywhere in the body can trigger the HPA axis to increase cortisol as an effort to reduce inflammation. This response also acts to suppress most other immune functions leaving one vulnerable to infections, viral activation and cancer. Clinicians should consider potential causes of inflammation that may be contributing to their patient’s stress response. The existence of chronic GI issues (infections, SIBO, food allergies, IBD), obesity, cardiovascular disease, joint pain, autoimmune disorders, airborne allergies, asthma and sinusitis should be revealed in an adequate history followed by appropriate testing to determine the cause. Removing sources of chronic inflammation reduces the need for cortisol and removes a key trigger in the HPA axis stress response.

**Treatment Options**

**Find Sources of Inflammation** – A good patient history and appropriate lab tests will reveal sources of inflammation. Treat each source of inflammation appropriately.

**Nutrient Support** – Supplementing with high-potency omega-3 fats, B-Complex, antioxidants and phytonutrients.

**Dietary Modification** – Remove nightshades (tomatoes, potatoes, eggplants, peppers), gluten, pasteurized dairy and refined sugar. Follow dietary recommendations listed above for glycemic control.

**Weight Loss** – Losing excess weight decreases inflammatory signaling and interrupts the cycle of metabolic disorders associated with glycemic dysregulation and hyperinsulinemia.

**Culinary Herbs that Decrease Inflammation** – Adding a variety of herbs and spices to our meals can have an anti-inflammatory effect. Consider adding: Turmeric, Cloves, Ginger, Rosemary, Sage, Thyme, Oregano, Marjoram, Cinnamon and Jamaican Allspice. Turmeric can be found in high potency capsules.

For more resources on HPA assessments, visit biohealthlab.com.