

Much of what we know about stress comes from the research of Dr. Hans Selye. Selye divided the human stress response into three stages:

**Alarm Stage:** This stage is the acute physiologic response to stress.

**Resistance Stage:** In this stage, the ability to adapt to stress starts to fail.

**Exhaustion Stage:** In this stage, the ability to mount a physiologic response to stress is impaired.

Selye's research focused on our physiologic responses to stress, but we now know that behavioural and affective responses to stress can also have a significant impact.

During conditions of stress, the adrenal glands, under the direction of the hypothalamus and pituitary glands, release cortisol, cytokines, catecholamines and neuropeptides. However, if the system is overworked and fails to shut down when stress abates, then the physiologic effects of stress can accumulate. This accumulation is called *high allostatic load*. Basically, chemical mediators of the stress response offer short-term benefits, but may cause damage if they remain active when no longer needed. A high

allostatic load is considered a risk factor for developing chronic illness.

Since more than 70% of disease is thought to be stress-related; identifying and treating individuals with a high allostatic load could potentially reduce the incidence of chronic disease. According to MacEwan, elevated or flattened diurnal cortisol rhythms and low dehydroepiandrosterone (DHEAS) to cortisol ratios are two primary indicators of a high allostatic load (along with inflammatory cytokines, elevated urinary cortisol and/or catecholamines).<sup>1</sup> A high allostatic load is considered a risk factor for developing chronic illness.

1. MacEwan B. Neuropsychopharmacol. 2002;22(2): 108-24

### Why Test Saliva Cortisol?

Saliva hormone testing is a non-invasive, simple way to map out the diurnal cortisol response. Repeatedly high salivary cortisol levels throughout the day may indicate hyperreactivity of the HPA axis, excessive glucocorticoid production, and an inability to adapt to continued stress. The body may compensate by inhibiting cortisol release, resulting in a flattened diurnal salivary cortisol profile. A flat cortisol profile protects against the damaging effects of high cortisol (e.g. breakdown of muscle and bone, increased blood glucose and hypertension) and reduces the allostatic load, but often results in debilitating symptoms of fatigue, feeling 'burned out' and 'tired but wired', depression, and decreased sex drive. In other words, even though low cortisol levels are physiologically protective, they can have a significant negative effect on how your patient feels.

By measuring diurnal cortisol profiles in saliva, healthcare professionals may identify individuals whose stress adaptation is compromised and

initiate appropriate treatment to restore health and quality of life.

- ▶ The diurnal variation of cortisol is readily mapped by using saliva testing since collection is easy to do at home or at work. Four specimens are obtained: morning (within first hour of waking), before lunch, before supper, and before bedtime. The cortisol levels for each point are graphed according to the reference range for that time period.
- ▶ Saliva is an excellent medium for measurement of cortisol because, unlike blood and serum where venipuncture can cause an anticipatory rise in cortisol, collection of saliva does not.
- ▶ An adrenal function panel can help motivate patients to make lifestyle changes. Many people recognize that they are under stress, but having a comparison to 'normal' can be a strong motivator to learn new coping skills.



### Cortisol DHEAS

The Adrenal  
Function Panel  
helps assess  
ability to cope  
with stress.



## Background on DHEAS

DHEA, or dehydroepiandrosterone, is also secreted by the adrenal glands. It is the most abundant steroid hormone in the body, circulating primarily in its sulfated form, DHEAS. DHEAS competes with cortisol at the receptor level, and balances the effects of cortisol. The ratio of cortisol to DHEAS tends to increase with age because DHEAS declines with age, while morning cortisol stays the same or increases slightly. A higher than expected ratio for a given age may be indicative of unbalanced adrenal function (cortisol too high or DHEAS too low). Factors contributing to imbalance may include acute or chronic stress, obesity, metabolic syndrome or diabetes, and hypothyroidism.

## Background on Cortisol

The adrenal glands produce cortisol 24 hours per day with a regular diurnal variation. Cortisol output is highest within the first hour after waking, declines steadily through the day, and reaches a low during sleep. Adrenal exhaustion tends to result in a flattened cortisol profile with loss of the morning surge, while earlier stages of the General Adaptation Syndrome generally result in one or more elevated cortisol points.

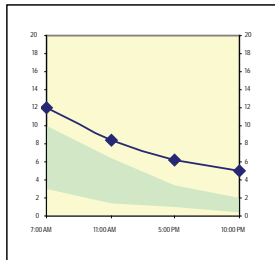
**Note:** Hair cortisol provides a longer-term view of cortisol production and is a convenient biological marker for chronic stress.

The following are some commonly observed patterns of adrenal dysfunction:

Cortisol Graph	Lifestyle Changes	Supplements to Consider
<p><b>Elevated Morning Cortisol</b></p>	<ul style="list-style-type: none"> <li>• Reduce stress and/or improve coping skills</li> <li>• Get adequate sleep</li> <li>• Eliminate caffeine</li> <li>• Reduce consumption of refined carbohydrates as they raise insulin levels, which lowers glucose, which triggers release of more cortisol (to raise glucose)</li> </ul>	<p><b>For Alarm/Resistance Stage</b></p> <ul style="list-style-type: none"> <li>• B-complex vitamins</li> <li>• Vitamin C</li> <li>• Magnesium</li> <li>• Calcium</li> <li>• Pantothenic acid</li> <li>• Trace minerals                             <ul style="list-style-type: none"> <li>– Zinc</li> <li>– Manganese</li> <li>– Selenium</li> <li>– Molybdenum</li> <li>– Chromium</li> <li>– Copper</li> <li>– Iodine</li> </ul> </li> <li>• Vitamin E</li> <li>• Adaptogens                             <ul style="list-style-type: none"> <li>– Ashwagandha</li> <li>– Cordyceps</li> <li>– Eleuthero</li> <li>– Panax ginseng</li> <li>– Rhodiola</li> <li>– Schisandra</li> </ul> </li> <li>• Magnolia officinalis, alone or in combination with other adrenally acting herbs</li> <li>• Phosphatidylserine</li> <li>• Omega-3 fish oils</li> <li>• Phytosterols (beta-sitosterol)</li> <li>• Theanine</li> <li>• Tyrosine</li> <li>• Phenylalanine</li> <li>• Methyl donors: MSM, SAME, betaine</li> </ul>
<p><b>Steep Drop in Cortisol</b></p>	<ul style="list-style-type: none"> <li>• A noon cortisol that is less than 40% of morning cortisol is suggestive of adrenal dysfunction even if points are within normal range.</li> <li>• Reduce stress and/or improve coping skills</li> <li>• Get adequate sleep</li> <li>• Eliminate caffeine</li> <li>• Reduce consumption of refined carbohydrates as they raise insulin levels, which lowers glucose, which triggers release of more cortisol (to raise glucose)</li> </ul>	
<p><b>Rebound Cortisol</b></p>	<ul style="list-style-type: none"> <li>• Patient experiences a 'rebound' in the afternoon</li> <li>• Reduce stress and/or improve coping skills</li> <li>• Get adequate sleep</li> <li>• Eliminate caffeine</li> <li>• Reduce consumption of refined carbohydrates as they raise insulin levels, which lowers glucose, which triggers release of more cortisol (to raise glucose)</li> <li>• Afternoon rise in cortisol may be due to increased activity or stress, e.g. driving home, exercise, eating.</li> </ul>	

## Cortisol Graph

### Chronically Elevated Cortisol



Probable Resistance Stage

## Lifestyle Changes

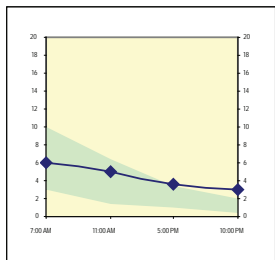
- Reduce stress and/or improve coping skills
- Get adequate sleep
- Eliminate caffeine
- Reduce consumption of refined carbohydrates as they raise insulin levels, which lowers glucose, which triggers release of more cortisol (to raise glucose)

## Supplement Rationale

### Supplements as per previous page

- **Vitamins and trace minerals** are required as cofactors in the synthesis of adrenal hormones. Excess stress can increase requirements for these nutrients.
- **Adaptogens** help the body adapt to high or low cortisol levels. They are helpful for all stages of the General Adaptation Syndrome.
- **Magnolia** helps bring down salivary cortisol levels and may have anxiolytic properties.
- **Phosphatidylserine** may help modulate elevated cortisol levels, particularly after exercise.
- **Omega-3** fish oil inhibits adrenal activation elicited by mental stress.
- **Phytosterols** help balance the ratio of cortisol to DHEAS.
- **Theanine** assists the brain in dealing with stressful events.
- The **amino acids** phenylalanine and tyrosine may accelerate the synthesis of adrenaline and noradrenaline.
- **Methyl donors** may help lower cortisol levels by assisting in the conversion of noradrenaline to adrenaline.

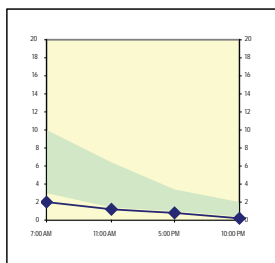
### Elevated Evening Cortisol



Probable Resistance Stage

- Reduce stress and/or improve coping skills
- Eliminate caffeine
- Reduce consumption of refined carbohydrates as they raise insulin levels, which lowers glucose, which triggers release of more cortisol (to raise glucose)
- High evening cortisol along with low DHEAS has been associated with increased breast cancer risk

### Adrenal Exhaustion



Exhaustion Stage

- Reduce stress and/or improve coping skills
- Get adequate sleep - may need to sleep later in morning
- Eliminate caffeine
- Reduce consumption of refined carbohydrates as they raise insulin levels, which lowers glucose, which triggers release of more cortisol (to raise glucose)
- Glass of salt water in the morning (use sea salt to taste)
- Mild to moderate exercise only
- Avoid potassium rich foods first thing in morning

- Adrenal gland concentrates are used on the assumption that naturally occurring precursors and polypeptides support the function of the hypothalamus and adrenals.
- Adrenal support vitamin/minerals:
  - B complex
  - High dose Vitamin C
  - Pantothenic acid
  - Calcium & Magnesium
  - Mixed tocopherols
- Adaptogens such as:
  - Ashwagandha
  - Cordyceps
  - Ginseng
  - Panax ginseng
  - Rhodiola
  - Schisandra
- Short-term supplementation with cortisol and intravenous trace element infusions may be required in some cases. (see *The Safe Uses of Cortisol* by William Jeffries, MD, F.A.C.P.)

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