The Adrenocortex Stress Profile (ASP) offers an assessment of the Hypothalamic-Pituitary-Adrenal (HPA) axis using carefully timed salivary samples of the hormones cortisol and DHEA. Clinicians have three options in HPA axis evaluation:

- **Adrenocortex Stress Profile (ASP):** Four salivary samples measured throughout the day to give insight into cortisol’s natural circadian diurnal rhythm.
- **Cortisol Awakening Response (CAR):** Three awakening samples to evaluate CAR and reflect HPA axis resiliency, and one evening cortisol sample, which has specific clinical associations.
- **Adrenocortex Stress Profile with Cortisol Awakening Response (ASP with CAR):** Six samples offering the most comprehensive look at cortisol and the HPA axis.

**The clinical interpretation of the Adrenocortex Stress Profile involves:**

1. Timed Cortisol Measurements
2. Overall Diurnal Rhythm/ Slope
3. Cortisol Awakening Response
4. DHEA
5. DHEA: Cortisol Ratio

**Timed Cortisol Measurements:**

Specific cortisol findings throughout a diurnal rhythm may be affected by any number of acute mental, emotional, and physical daily stressors. Abnormal results should be correlated with each patient’s clinical presentation and daily routine.\(^1\)\(^4\)

<table>
<thead>
<tr>
<th>TIMING</th>
<th>SIGNIFICANCE</th>
<th>CONSIDERATIONS WHEN HIGH</th>
<th>CONSIDERATIONS WHEN LOW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol Awakening Response (CAR)</td>
<td>HPA axis resiliency</td>
<td>Adaptive anticipation of daily stress</td>
<td>Burnout, depression, PTSD, chronic fatigue syndrome, early loss experiences, material hardship, amnesia, hippocampal damage, non-response, abnormal sampling(^2)(^6)(^8)</td>
</tr>
<tr>
<td></td>
<td>Perception of control around chronic stress(^5)</td>
<td>Stimulation of motor function, immune response, and alertness(^6)(^7)</td>
<td></td>
</tr>
<tr>
<td>Morning 7:00AM-9:00AM</td>
<td>Peak ACTH-mediated adrenal gland response</td>
<td>Exercise, blood sugar dysregulation, lifestyle stressors, pain</td>
<td>Inability to mount peak response due to HPA axis dysfunction and/or down regulation from chronic stressors</td>
</tr>
<tr>
<td>Midday 11:00AM-1:00PM</td>
<td>Adaptive function of the HPA axis to daily routine</td>
<td>Exercise, blood sugar dysregulation, lifestyle stressors, pain</td>
<td>HPA axis dysfunction</td>
</tr>
<tr>
<td>Afternoon 3:00PM-5:00PM</td>
<td>Can reflect glycemic control</td>
<td>Exercise, blood sugar dysregulation, lifestyle stressors, pain</td>
<td>HPA axis dysfunction</td>
</tr>
</tbody>
</table>
The natural cortisol diurnal rhythm shows a peak within the first hour after awakening, a rapid decline over the morning hours, and then tapering through the rest of the day before reaching its lowest point at night.\(^1\)

### Normal Diurnal Slope

The natural cortisol diurnal rhythm shows a peak within the first hour after awakening, a rapid decline over the morning hours, and then tapering through the rest of the day before reaching its lowest point at night.\(^1\)

### Low Slope

- Chronic stress burden
- Poor psychosocial function
- Lack of HPA axis resiliency
- Lower perceived control over stress
- Post-Traumatic Stress Disorder (PTSD)
- Persistent fatigue, anxiety, and depression
- Predictive of health outcomes, such as increased breast cancer mortality, increased coronary calcifications, and increased body mass index\(^1,3\)

### High Slope

- Appropriate response to a major stressor
- Perceived insurmountable challenge\(^2\)

### Treatment Options:

Treatment of abnormal cortisol should be directed at the stressor’s root cause. Lifestyle modification with relaxation methods, dietary changes, pain management, and overall HPA axis support with nutrition, adaptogens, and supplements can be helpful.\(^14\)
Cortisol Awakening Response (CAR)

CAR reflects a person's ability to cope with anticipated challenges and the perceptions of control around chronic stress. CAR is the change in cortisol from waking to 30 minutes, expressed as a percentage. A value of at least 50% is expected.\textsuperscript{3,5,6,15}

Blunted CAR

- Burnout
- Depression
- PTSD
- Chronic Fatigue Syndrome
- Self-reported health problems
- Early loss experiences
- Material hardship
- Amnesia
- Hippocampal damage\textsuperscript{6,7}

Elevated CAR

- Adaptive anticipation of daily stressors (“preparing for action”)
- Stimulation of motor function, immune response, and alertness\textsuperscript{6,7}
Negative CAR

- Ensure there was no delay between waking and obtaining the first sample
- Literature is evolving regarding clinical implications\(^\text{16,17}\)
- One hypothesis is that a negative CAR percentage may reflect a blunted CAR with further loss of resiliency

\[ \text{Waking} \quad 30 \text{ minutes} \quad 7\text{AM} - 9\text{AM} \]

\[ \begin{align*}
0.440 & \quad 0.220 & \quad 0.150 \\
\text{Increase After Waking} & \quad \text{Expected:} & \quad \text{>50\%} \\
30 \text{ min - waking expressed as \%} & \end{align*} \]

CAR Non-Response

- 25% of healthy adults do not mount a CAR
- Response is defined as an increase of at least 0.09µg/dL above individual baseline with otherwise adequate cortisol diurnal curve
- Ensure proper sampling\(^\text{5,8}\)

\[ \text{Waking} \quad 30 \text{ minutes} \quad 7\text{AM} - 9\text{AM} \]

\[ \begin{align*}
0.220 & \quad 0.100 & \quad 0.000 \\
\text{Increase After Waking} & \quad \text{Expected:} & \quad \text{>50\%} \\
30 \text{ min - waking expressed as \%} & \end{align*} \]

CAR Elevated with High Slope

- General HPA axis dysfunction
- Significant stressor, real or perceived\(^\text{15,18}\)

\[ \text{Waking} \quad 30 \text{ minutes} \quad 7\text{AM} - 9\text{AM} \]

\[ \begin{align*}
0.560 & \quad 0.360 & \quad 0.260 \\
\text{Increase After Waking} & \quad \text{Expected:} & \quad \text{>50\%} \\
30 \text{ min - waking expressed as \%} & \end{align*} \]

CAR Elevated with Elevated Slope

- Anticipation and reflection of daily stress
- Overall total cortisol levels during CAR are predictive of relative mean cortisol levels throughout the day\(^\text{15,19}\)
**DHEA**

**HIGH:** Exogenous exposure, supplementation, polycystic ovary syndrome, adrenal hyperplasia, and adrenal tumors

**LOW:** Advancing age, chronic stress, HPA axis dysfunction

Low DHEA levels have been associated with immune dysregulation, cardiovascular disease, arthritis, osteoporosis, insomnia, declining cognition, depression, fatigue, and decreased libido.\(^{20-24}\)

**DHEA: Cortisol Ratio**

**HIGH:** Favors anabolic activity
Address specific cortisol and DHEA abnormalities\(^{21,25,26,27}\)

**LOW:** Favors catabolic activity
Address specific cortisol and DHEA abnormalities\(^{21,25,26,27}\)

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**CAR Blunted with Low Slope**

- Generalized HPA axis dysfunction
- Burnout
- Chronic stressor\(^ {15,19}\)
References


