Nordic Laboratories

PATIENT: XXXXXXXXXXXXXXXXX			TEST REF: TST-NL-XXXX
TEST NUMBER: T-NL-XXXXX (XXXXXXXXXX)	COLLECTED: XX/XX/XXXX		PRACTITIONER: XXXXXXXXXXXXX
GENDER: XYZ	RECEIVED: XX/XX/XXXX		
AGE: XX	TESTED: XX/XX/XXXX		XXXXXXXXXXXXXXXXXXXX

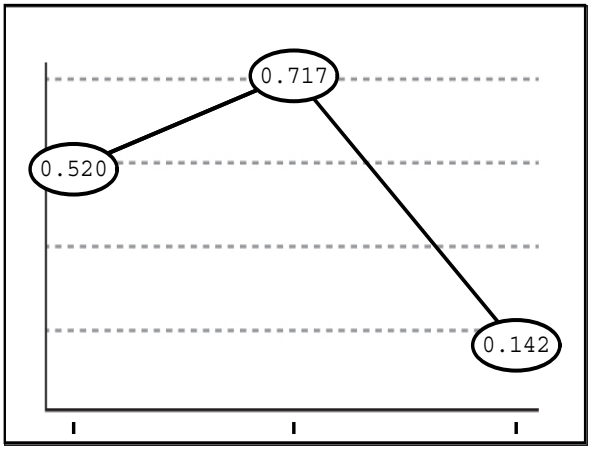
TEST NAME: Adrenocortex Stress Profile with CAR

4300 Adrenocortex Stress Profile - Saliva

Methodology: EIA

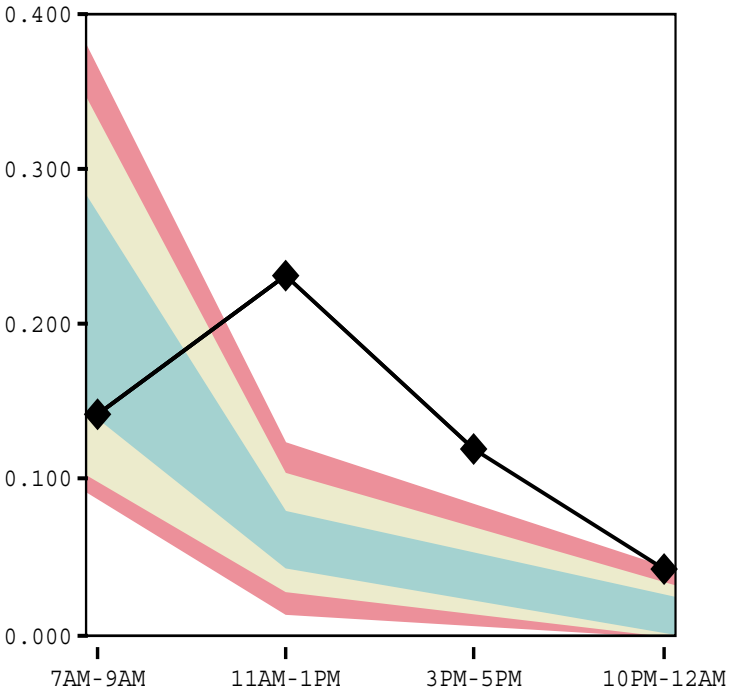
Cortisol, Cortisol Awakening Response, and DHEA

Cortisol Awakening Response



Percent Increase	38	Expected: >= 50 %

Salivary Cortisol



DHEA

		Reference Range
DHEA 7AM - 9AM♦	296	71-640 pg/mL

		Reference Range
DHEA: Cortisol Ratio/10,000♦	2,085	358-2,538

Results

	Waking	30 minutes	7AM - 9AM*	11AM - 1PM*	3PM - 5PM*	10PM - 12AM*
Patient Result (mcg/dL) >>	**0.520**	**0.717**	**0.142**	**0.231**	**0.119**	**0.042**
Reference Range (mcg/dL) *Based on Collection Times	N/A	N/A	0.097-0.337	0.027-0.106	0.013-0.068	<=0.034
Actual Collection Time	6:12AM	6:47AM	8:14AM	11:34AM	4:04PM	11:38PM

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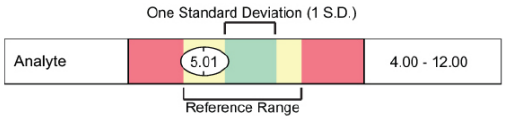
Commentary

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or as treatment recommendations. Diagnosis and treatment decisions are the practitioner's responsibility.

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. All assay have been cleared by the U.S. Food and Drug Administration, unless otherwise noted with ◆.

The **Reference Range** is a statistical interval representing 95% or 2 Standard Deviations (2 S.D.) of the reference population.

One Standard Deviation (1 S.D.) is a statistical interval representing 68% of the reference population. Values between 1 and 2 S.D. are not necessarily abnormal. Clinical correlation is suggested. (See example below)



Diurnal Cortisol Rhythm/Slope

The natural cortisol diurnal rhythm shows a peak within the first hour after awakening, a rapid decline over the morning hours, and then a tapering through the rest of the day before reaching a nighttime nadir.

A flat slope is characterized by low morning levels, blunted afternoon response and/or evening drop in cortisol levels. Flattened slopes are:

- Associated with a chronic stress burden, poor psychosocial functions, lack of HPA axis resiliency and lower perceived control over stress.
- Predictive of health outcomes, such as increased breast cancer mortality, increased coronary calcifications, and increased body mass index.
- Seen in Post-Traumatic Stress Disorder (PTSD), persistent fatigue, anxiety, depression, and Addison's Disease.

A "high flat" slope is characterized by high morning levels that fail to show a diurnal decrease.

- They can be a normal/appropriate response to a major stressor.
- High flat slopes might also suggest a challenge that seems insurmountable.

Timed Cortisol Measurements

Specific cortisol elevations throughout a diurnal rhythm may be caused by any number of acute mental, emotional and physical daily stressors, blood sugar dysregulation, exercise or pain. Abnormal results should be correlated with each patient's clinical presentation and specific daily routine.

Morning (7:00 AM – 9:00 AM) cortisol measurement reflects peak ACTH-mediated adrenal gland response.

- Exaggerated levels can be seen with exercise, blood sugar dysregulation, daily stressors, pain, and underlying adrenal hyperplasia or Cushing's syndrome.
- Low levels may reflect an inability to mount a peak response as is seen in adrenal dysfunction and/or down regulation from chronic stressors.

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Mid-morning (11:00 AM – 1:00 PM) cortisol levels reflect an adaptive function of the HPA axis to daily routine.

- Elevated levels should be correlated with daily stressors, such as exercise, blood sugar dysregulation, perceived and actual lifestyle stressors and pain.
- Lower levels can reflect HPA axis dysfunction.

Afternoon (3:00 PM – 5:00 PM) cortisol is often reflective of glycemic control due to the post-prandial timing of collection.

- Elevated levels can reflect any number of daily stressors as previously outlined.
- Low levels can reflect underlying HPA axis dysfunction.

Evening (10:00 PM – 12:00 AM) cortisol levels are a good indication of baseline HPA axis function since they represent the lowest level during the circadian rhythm.

- Elevated levels may be due to stress, exercise, alcohol, and specific lifestyle stressors.
- Elevated evening salivary cortisol is linked to insomnia
- High evening cortisol levels are also associated with various diseases such as diabetes, cardiovascular disease, hormonally driven cancers, and osteoporosis.

Treatment of elevated cortisol should be directed at the root cause of the stressor. Lifestyle modification with relaxation methods, dietary changes, pain management, and overall HPA axis support with nutrition and/or adaptogens can be helpful. Glandulars may be added if additional support is necessary.

Cortisol Awakening Response (CAR)

CAR is calculated by a direct percent increase: difference between 30 minutes and wake, divided by wake, then multiplied by 100. In literature, there are several ways to calculate CAR. Expected increases may differ depending on which calculation is used. Most literature demonstrates an expected increase of greater than 50% as a reflection of HPA axis resiliency.[1]

CAR represents the momentum of rising cortisol levels that begins several hours prior to awakening and an additional transient increase. The initial cortisol rise begins due to ACTH-mediated normal HPA axis activities with the additional CAR increase caused by supra-chiasmic nucleus (SCN) light activation.

CAR reflects a person's ability to cope with anticipated challenges and the perceptions of control around chronic stress. CAR is calculated based on the percent cortisol rise from awakening to 30 minutes. A value of approximately 50% is expected.

Approximately 25% of healthy adults do not mount a CAR, and are termed non-responders. Response is defined as an increase of at least 2.5 nmol/l (0.09 mcg/dL) above individual baseline. Any patient with a result less than this is considered a "non-responder" if sampling was performed correctly and the rest of the diurnal curve shows adequate cortisol response.

- Blunted CAR is seen in clinical burnout, self-reported health problems, early loss experiences, material hardship, depression, PTSD, and amnesia.
- Elevated CAR can be adaptive as a reflection of anticipation for daily stress. It may play a literal role in "preparing for action" by stimulating motor function, immunity responses, and alertness.

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- If CAR is abnormal, and the rest of the diurnal pattern is not, then this would imply that a CAR-specific mechanism (SCN-related signaling) is implicated instead of a CRH or ACTH-mediated mechanism. Any abnormality of the hippocampus may blunt the CAR response and not affect the diurnal slope.

- If both the CAR and the diurnal rhythm are abnormal, this may represent a more general HPA dysfunction. It may also be useful to look at DHEA for a complete assessment of the HPA axis.

CAR treatment involves HPA axis and adrenal support using lifestyle modification, nutrition and adaptogens. However, insight into blunted or elevated CAR may help direct additional modalities such as behavioral modification and psychological therapies.

Evening (10:00 PM – 12:00 AM) cortisol levels are a good indication of baseline HPA axis function since they represent the lowest level during the circadian rhythm.

- Elevated levels may be due to stress, exercise, alcohol, and specific lifestyle stressors.
- Elevated evening salivary cortisol is linked to insomnia.
- High evening cortisol levels are also associated with various diseases such as diabetes, cardiovascular disease, hormonally driven cancers, and osteoporosis.

DHEA

DHEA levels peak at around age 25, then decline steadily through the following decades. DHEA can be converted downstream in the steroidogenic pathway to create androgens and estrogens. It has antioxidant and anti-inflammatory properties and can be protective against corticosterone's neurotoxic effects.

- Lower levels of DHEA are seen with advancing age and have been associated with immune dysregulation, cardiovascular disease, arthritis, osteoporosis, insomnia, declining cognition, depression, fatigue, and decreased libido.
- Elevated levels of DHEA may reflect endogenous exposure and supplementation. Other considerations include Polycystic Ovarian Syndrome (PCOS,) adrenal hyperplasia and adrenal tumors.

General recommendations include overall control of the cortisol response, HPA axis support using nutrition, adaptogens, and behavioral modification.

DHEA:Cortisol Ratio

This calculation represents anabolic and catabolic balance. Since DHEA acts not only as an anabolic hormone, but appears to down-regulate the cellular effects of cortisol, this measurement can theoretically enhance the predictive value of HPA axis dysfunction.

- An elevated ratio reflects elevated DHEA levels as compared to cortisol, which favors anabolic activity. Causes of DHEA and cortisol abnormalities should be evaluated.
- A decreased ratio generally reflects a more catabolic state. It is associated with cortisol elevations and HPA-axis imbalances. Causes of DHEA and cortisol abnormalities should be addressed.
- An optimal ratio indicates proper HPA axis homeostasis.

References:

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Commentary

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2. Stalder T, Kirschbaum C, Kudielka BM, et al. Assessment of the cortisol awakening response: Expert consensus guidelines. *Psychoneuroendocrino.* 2016;63:414-432.
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