



Patient: **SAMPLE**
PATIENT

DOB:

Sex:

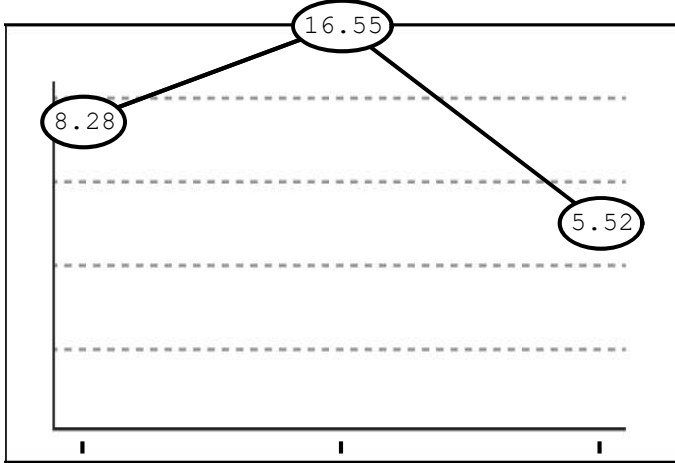
MRN:

4116 Cortisol Awakening Response

Methodology: EIA

Salivary Cortisol, Cortisol Awakening Response, and DHEA

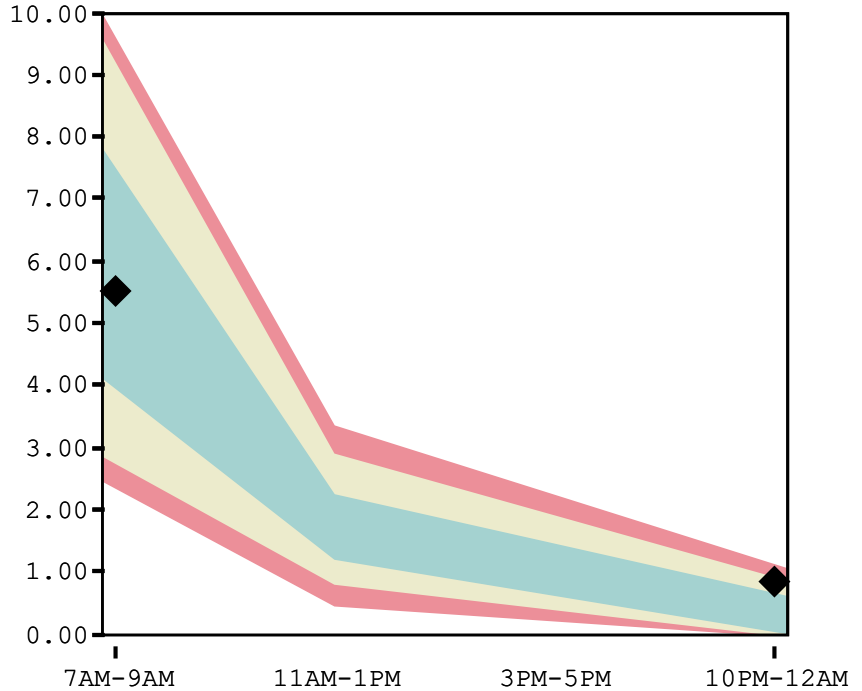
Cortisol Awakening Response



Waking 30 minutes 7AM - 9AM

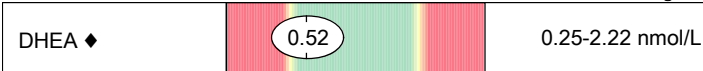
Percent Increase **Expected:**
>= 50 %

Salivary Cortisol

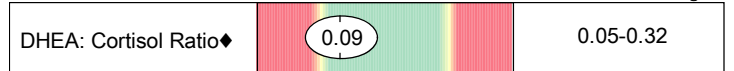


DHEA

Reference Range



Reference Range



Results

	Waking	30 minutes	7AM-9AM*	10PM-12AM*
Patient Result (nmol/L) >>	8.28	16.55	5.52	0.83
Reference Range (nmol/L) *Based on Collection Times	N/A	N/A	2.68-9.30	<=0.94
Actual Collection Time	7:10AM	7:40AM	9:00AM	10:00PM



Secretary IgA Results

Analyte	Reference Range (µg/mL)
Secretary IgA◆	56-212

100

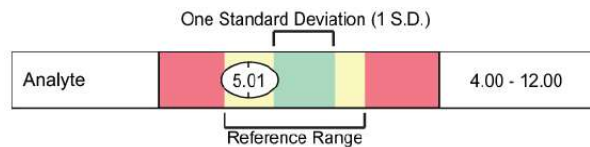
Commentary

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)



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-chiasmatic 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

Commentary

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.
- 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.

Sample 4 (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. Specific

Commentary

cortisol and DHEA abnormalities should be evaluated as outlined previously.

- A decreased ratio generally reflects a more catabolic state. It is associated with cortisol elevations and HPA-axis imbalances. Specific cortisol and DHEA abnormalities should be addressed.
- An optimal ratio indicates proper HPA axis homeostasis.

References:

1. Saxbe DE. A field (researcher's) guide to cortisol: tracking HPA axis functioning in everyday life. *Health Psychol Rev.* 2008;2(2):163-190.
2. Maninger N, Wolkowitz OM, Reus VI, Epel ES, Mellon SH. Neurobiological and neuropsychiatric effects of dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS). *Front Neuroendocrinol.* 2009;30(1):65-91.
3. Pluchino N, Drakopoulos P, Bianchi-Demicheli F, Wenger J, Petignat P, Genazzani A. Neurobiology of DHEA and effects on sexuality, mood and cognition. *J Steroid Biochem Mol Biol.* 2015;145:273-280.
4. Clow A, Hucklebridge F, Thorn L. The cortisol awakening response in context. *Int Rev Neurobiol.* 2010;93:153-175.
5. Stalder T, Kirschbaum C, Kudielka BM, et al. Assessment of the cortisol awakening response: Expert consensus guidelines. *Psychoneuroendocrinology.* 2016;63:414-432.
6. Wust S, Wolf J, Hellhammer DH, Federenko I, Schommer N, Kirschbaum C. The cortisol awakening response-normal values and confounds. *Noise health.* 2000;2(7):79.
7. Fries E, Dettenborn L, Kirschbaum C. The cortisol awakening response (CAR): facts and future directions. *Int J Psychophysiol.* 2009;72(1):67-73.

Secretory immunoglobulin A (sIgA)

Methodology: Immunoturbidimetric

Secretory immunoglobulin A (sIgA) is the dominant immunoglobulin in external secretions that cover the mucosal surfaces (respiratory and gastrointestinal). It is a vital component of the immune system's "first line of defense" against pathogenic microorganisms. sIgA production is affected by a number of factors including stress, emotions, nutritional status, commensal bacteria, pathogens, and inflammation.

Elevated levels of salivary sIgA reflect an immune response to stimulation, such as stress, inflammation, and infection. Acute psychological stress, real and perceived, is associated with increases in sIgA concentration and secretion rate.

Lower salivary secretory IgA levels are seen in chronic stress or excessive exercise. Levels of salivary secretory IgA can decline with advanced age.

References:

1. Jarfarzadeh A, Sadeghi M, et al. Salivary IgA and IgE levels in healthy subjects: relation to age and gender. *Braz Oral Res.* 2010;24(1):21-27.
2. Tsujita S, Morimoto K. Secretory IgA in saliva can be a useful stress marker. *Environ Health Prev Med.* 1999;4(1):1-8.
3. Phillips AC, Carroll D, Evans P, et al. Stressful life events are associated with low secretion rates of immunoglobulin A in saliva in the middle aged and elderly. *Brain Behav Immun.* 2006;20(2):191-197.
4. Engeland C, Hugo F, Hilgert J, et al. Psychological distress and salivary secretory immunity. *Brain Behav Immun.* 2016;52:11-17.
5. Fahlman MM, Engels HJ, Hall H. sIgA and Upper Respiratory Syndrome During a College Cross Country Season. *Sports Med Int Open.* 2017;1(06):E188-E194.