

Functional Medicine University's Functional Diagnostic Medicine Training Program

INSIDER'S GUIDE ADRENAL stress index interpretation

By Ron Grisanti, D.C. & Dicken Weatherby, N.D.

<http://www.FunctionalMedicineUniversity.com>

Limits of Liability & Disclaimer of Warranty

We have designed this book to provide information in regard to the subject matter covered. It is made available with the understanding that the authors are not liable for the misconception or misuse of information provided. The purpose of this book is to educate. It is not meant to be a comprehensive source for the topic covered, and is not intended as a substitute for medical diagnosis or treatment, or intended as a substitute for medical counseling. Information contained in this book should not be construed as a claim or representation that any treatment, process or interpretation mentioned constitutes a cure, palliative, or ameliorative. The information covered is intended to supplement the practitioner's knowledge of their patient. It should be considered as adjunctive support to other diagnostic medical procedures.

This material contains elements protected under International and Federal Copyright laws and treaties. Any unauthorized reprint or use of this material is prohibited

Contents

Cortisol/DHEA Review	3
Cortisol Rhythm (4 Timed Samples)	3
Stress and Cortisol	3
DHEA-S Average (Value of 2 samples)	4
The Significance of the Cortisol/DHEA Ratio	5
Pregnenolone Steal.....	6
The Efficacy of Salivary Hormone Testing.....	7
Functional Adrenal Stress Profile.....	11
Stage I Adrenal Exhaustion.....	12
Phases of Adaptation.....	14
Stage II Adrenal Exhaustion.....	19
Stage III Adrenal Exhaustion.....	21
Adrenal/DHEA Restoration.....	27

Cortisol/DHEA Review

The adrenal glands produce complementary hormones **cortisol** and **dehydroepiandrosterone (DHEA)**. Cortisol and DHEA are involved in the physiology of virtually every cell.

Cortisol Rhythm (4 Timed Samples)

Features of Cortisol include:

- ❖ Stimulating **gluconeogenesis**, and it is essential for normal **glycogenolysis**.
- ❖ Cortisol affects the heart, vasculature, blood pressure, water excretion, and electrolyte balance.
- ❖ It mobilizes protein stores in all tissues except liver; it mobilizes fatty acids from adipose
- ❖ It is the precursor of cortisone and acts as an anti-inflammatory; and
- ❖ It is the primary hormone directing immune function.
- ❖ Cortisol can either stimulate or inhibit gene transcription, it promotes apoptosis, and it affects bone and calcium dynamics.
- ❖ It affects behavior, mood, neural activity, and a variety of central nervous system biochemical processes.
- ❖ Cortisol affects the eyes, gastrointestinal tract, reproductive function, and the production and clearance of other classes of hormones.
- ❖ The general effect of **excess cortisol is usually catabolic**.

Stress and Cortisol

In the presence of stressors, the body almost immediately attempts to increase cortisol levels. This increase is associated with both an endocrine and an autonomic response in preparing the body to defend itself.

Elevated cortisol levels for extended periods, however, negatively affect virtually every aspect of physiology. It becomes more difficult to maintain proper blood sugar levels, to slow down for rest, recovery, and repair, to get good quality sleep, to balance other hormones, to maintain mucosal surface integrity, to maintain bone mass, to produce effective immune function, to effectively regulate inflammatory processes, or to detoxify the body.

Without proper intervention, continued adrenal hyperstimulation can lead to adrenal exhaustion, and eventually adrenal failure can occur. The degree and timing of various cortisol imbalances provide the health professional with invaluable insight into the nature of the causative stressors, and allow the practitioner to formulate a remedial protocol.

DHEA-S Average (Value of 2 samples)

DHEA is the major precursor of testosterone and the estrogens. The more active, sulfate form of DHEA is DHEA-S, which provides a more reliable measure of DHEA levels. We report the average of two DHEA-S values, taken between **12-1 pm, and between 4-5 pm.**

The normal DHEA-S level is 2.0-10.0 ng/ml, and the ideal is **7.0-8.0 ng/ml.**

DHEA is an important modulator of many physiological processes. It promotes the growth and repair of protein tissue, especially muscle, and acts as a counter-regulatory agent to cortisol, negating many of the harmful effects of excess cortisol.

Over extended periods of an increased demand for cortisol, DHEA levels decline, and DHEA is then no longer able to counter-regulate the negative effects of excess cortisol.

Depressed DHEA levels serve as an early warning of potential adrenal exhaustion.

A chronic imbalance between adrenal stimulation and cortisol and/or DHEA output is associated with a multitude of both clinical and subclinical systemic disorders, some of which are listed below.

Chronically depressed DHEA results in an imbalance in sex hormones.

Abnormal cortisol and/or DHEA values, either elevated or depressed, result in decreased activity of the immunocytes that produce secretory IgA (sIgA). SIgA provides a mucosal first-line immune defense against virtually every pathogen, including parasites, protozoa, yeasts, fungi, bacteria, and viruses. SIgA also protects against inflammatory reactions to food antigens. Dysfunctional mucosal immunity is associated with an increased risk of infections and of adverse food reactions.

Supplementary Factors

Readily identifiable inducers of increased adrenal stimulation include stressors such as tissue damage, inflammation, pain, and mental or emotional stress.

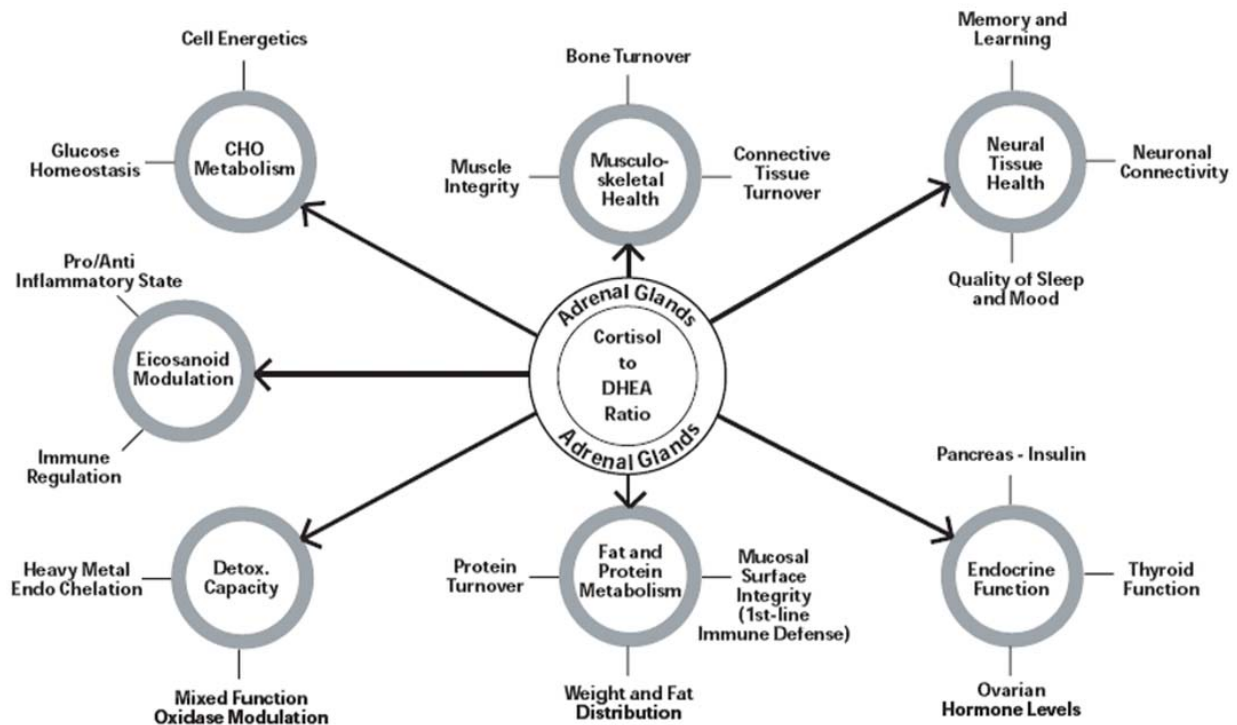
Other significant physiological stressors can be subclinical, and include intolerance to the gliadin fraction of gluten protein, lactose or sucrose intolerance, glycemic dysregulation, delayed food sensitivity, and the presence of parasites or pathogens.

Additional testing may be necessary to rule out the possibility of these and other ancillary factors interfering with digestion and absorption. This type of problem could likely impede such fundamental and critical processes as the ability to absorb water, the assimilation of essential nutrients, and the maintenance of normal blood sugar.

Chronic dysfunction of any of these processes is a sufficient cause of adrenal exhaustion. Physiological pathways, organs, or systems identified as being the major cause of some other disorder may concurrently serve as causative agents in adrenal exhaustion.

In most cases, regardless of the priority given to another pathway, organ, or system as being dysfunctional, and virtually regardless of the condition identified, adrenal exhaustion resulting from excessive stress must not be tolerated and must be addressed.

The Significance of the Cortisol/DHEA Ratio

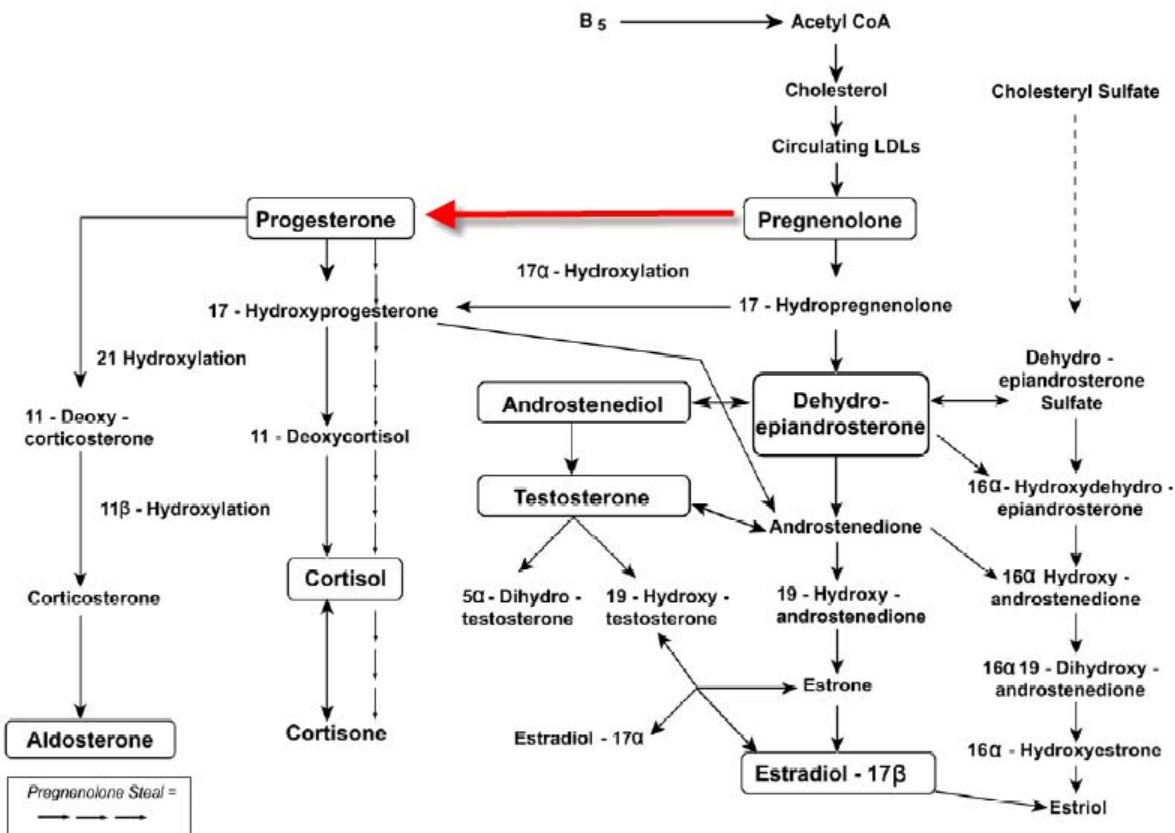


© 2004 - BioHealth Diagnostics

Cortisol is the primary hormone that directs immune function and is involved in virtually all aspects of body function. Both cortisol and DHEA have genetic influences. When cortisol and DHEA work together in harmony (maintaining a **normal ratio of 5:1 to 6:1** between cortisol and DHEA), the body is then said to be in a normal state of adaptation to stress.

When unable to maintain this normal state of adaptation the body can now enter into a state of maladaptation to stress. This is now referred to as a chronic stress response, i.e. pregnenolone steal/cortisol escape/elevated cortisol to DHEA ratio. The longer one stays in a state of chronic stress the more compromised all aspects of body function become. This can ultimately result in hormone, immune and metabolic systems breakdown.

Pregnenonolone Steal



© 2004 - BioHealth Diagnostics

A physiological response to stress, with shifting of the steroidogenic pathway to cortisol at the expense of DHEA.

The body's preferential pathway under chronic stress is called **Pregnenolone Steal or Cortisol Escape.**

When the body is in a “chronic stress response”, pregnenolone, the precursor to all the rest of the steroidal hormones, is diverted (see arrows) to cortisol – cortisone. This is at the detriment of all the other steroidal hormones; i.e. progesterone, aldosterone (mineral/cortical pathway/sodium-potassium pump), DHEA and its metabolites: the sex hormones, estrogens and testosterone. As pregnenolone is diverted to cortisol-cortisone, DHEA depletion begins.

The result is a depressed **cortisol to DHEA ratio**. This is measurable with the Functional Adrenal Stress Profile. Simply divide the total of cortisol by the DHEA(s) average to get the ratio. Again the **normal ratio is approximately 5:1 to 6:1**.

The Efficacy of Salivary Hormone Testing

Over the last few years experts in conventional medical research have shown increasing support for using salivary assays in the diagnosis and prevention of disease. In March 2005, the National Institutes of Health in Bethesda, MD, funded 10 groups nationwide to advance saliva testing.

Unlike blood or urine hormone testing, saliva analysis assesses the **biologically active compounds** that are active at the cellular level. In addition, salivary hormone analysis enables the clinician to have the patient collect multiple samples over the course of a day. This represents what is **clinically relevant** revealing the patient's true hormonal activity.

Unfortunately, blood serum cortisol is mostly **protein bound** which means about 1-10% of the steroids in the blood are in unbound, or free form. The rest approximately 93-99% of the total are bound to carrier proteins such as cortisol-binding globulin, sex hormone-binding globulin, and albumin which is **biologically unavailable**. Since only unbound steroids can freely diffuse into various target tissues in the body, they are the only hormones that are considered **biologically active**. **Saliva testing measures the free-circulating, biologically active hormones**. Measuring the concentration of nonbioavailable forms in urine or serum is irrelevant since the data is insufficient as to the concentration of the more clinically significant free hormones in circulation found in saliva.

As a diagnostic fluid, saliva is the most convenient, non-invasive specimen available for the patient. Invasive procedures, such as blood draws, are not just extremely impractical and costly when it comes to acquiring multiple samples; they also cause a stressful event on the body which can promote a release of cortisol, thus skewing the result for one event.

	Salivary Cortisol	Serum Cortisol	Urine Cortisol
Real Life Adrenal Evaluation	Multiple salivary specimens. Can be collected under real life situations ; at home, at work	Serum collection requires clinic visit and creates apprehension due to anticipation of venipuncture. This may blur the results by causing an artificial increase in cortisol. Does not take into account real life conditions. Best used for advanced adrenal diseases such as Addison's and/or Cushing's.	24 hour urine test has metabolites of the hormones and is not time specific and does not reflect time sensitive hormonal and stress responses.
Time Specific	Multiple saliva samples collected at different times allows evaluation of hormonal stress response and circadian	The routine single serum sample does not allow circadian cycle evaluation , i.e., no real	24 hour urine is absolutely time non-specific and does not reflect circadian rhythm at all

	cycle	time component	
BioActive Hormone Fraction	Salivary cortisol reflects the unbound bioactive hormone level to which living cells are subjected	Routine serum hormone testing reflects the total hormone level not the bioactive fraction . Total levels are crude estimates of unbound bioactive hormones	Urine hormones reflect production and catabolism and do not reflect tissue level hormone concentrations that living cells are exposed to leading to the potential of misleading interpretations
Therapeutic Discrimination	Because the ASI can sub classify adrenal dysfunction into time related values, therapeutic option are expanded and treatments are very specific	With serum and urine testing, results are reported as high, low or normal. Hormone values and treatment options are limited and not always synchronized and harmonious with the natural circadian cycle of the patient . This is a very crude approach to therapy	

Do not have patient do testing when in NOT in a normal environment. Testing should be performed during the patient's basic normal daily activities to accurately reflect how stress is impacting the patient's cortisol output.

1: [Ann Clin Biochem](#). 1983 Nov;20 (Pt 6):329-35.

Salivary cortisol: a better measure of adrenal cortical function than serum cortisol.

[Vining RE](#), [McGinley RA](#), [Maksvytis JJ](#), [Ho KY](#).

Salivary cortisol concentration was found to be directly proportional to the serum unbound cortisol concentration both in normal men and women and in women with elevated cortisol-binding globulin (CBG). The correlation was excellent in dynamic tests of adrenal function (dexamethasone suppression, ACTH stimulation), in normals and patients with adrenal insufficiency, in tests of circadian variation and randomly collected samples. Women in the third trimester of normal pregnancy exhibited elevated salivary cortisol throughout the day. The relationship between salivary and serum total cortisol concentration was markedly non-linear with a more rapid increase in salivary concentration once the serum CBG was saturated. The rate of equilibrium of cortisol between blood and saliva was very fast, being much less than 5 minutes. These data, combined with a simple, stress-free, non-invasive collection procedure, lead us to suggest that salivary cortisol is a more appropriate measure for the clinical assessment of adrenocortical function than is serum cortisol.

PMID: 6316831 [PubMed - indexed for MEDLINE]

Salivary cortisol determined by enzyme immunoassay is preferable to serum total cortisol for assessment of dynamic hypothalamic-pituitary-adrenal axis activity.

[Gozansky WS](#), [Lynn JS](#), [Laudenslager ML](#), [Kohrt WM](#).

Division of Geriatric Medicine, Department of Medicine, University of Colorado at Denver and Health Sciences Center, Denver, CO 80262, USA. wendee.gozansky@uchsc.edu

OBJECTIVE: The aim of this study was to determine whether salivary cortisol measured by a simple enzyme immunoassay (EIA) could be used as a surrogate for serum total cortisol in response to rapid changes and across a wide range of concentrations. **DESIGN:** Comparisons of matched salivary and serum samples in response to dynamic hypothalamic-pituitary-adrenal (HPA) axis testing. **Subjects** Healthy women (n=10; three taking oral oestrogens) and men (n=2), aged 23--65 years, were recruited from the community. **Measurements** Paired saliva and serum samples were obtained during three protocols: 10 min of exercise at 90% of maximal heart rate (n=8), intravenous administration of corticotrophin-releasing hormone (CRH; n=4), and dexamethasone suppression (n=7). Cortisol was measured in saliva using a commercial high-sensitivity EIA and total cortisol was measured in serum with a commercial radioimmunoassay (RIA). **Results** The time course of the salivary cortisol response to both the exercise and CRH tests paralleled that of total serum cortisol. Salivary cortisol demonstrated a significantly greater relative increase in response to the exercise and CRH stimuli (697+/- 826% vs. 209+/- 150%, P=0.04 saliva vs. serum). A disproportionately larger increase in free cortisol, compared with total, would be expected when the binding capacity of cortisol-binding globulin (CBG) is exceeded. In response to dexamethasone suppression, relative decreases in cortisol were not significantly different between the two media (-47+/- 56% vs. -84+/- 8%, P=0.13 saliva vs. serum). Although a significant linear correlation was found for all paired salivary and serum total cortisol samples (n=183 pairs, r=0.60, P<0.001), an exponential model provided a better fit (r=0.81, P<0.001). The linear correlations were strengthened when data from subjects on oral oestrogens (n=52 pairs, r=0.75, P<0.001) were separated from those not taking oestrogens (n=131 pairs, r=0.67, P<0.001). **Conclusions** Salivary cortisol measured with a simple EIA can be used in place of serum total cortisol in physiological research protocols. Evidence that salivary measures represent the biologically active, free fraction of cortisol includes: (1) the greater relative increase in salivary cortisol in response to tests that raise the absolute cortisol concentration above the saturation point of CBG; (2) the strong exponential relationship between cortisol assessed in the two media; and (3) the improved linear correlations when subjects known to have increased CBG were analysed separately. Thus, an advantage of measuring salivary cortisol rather than total serum cortisol is that it eliminates the need to account for within-subject changes or between-subject differences in CBG.

PMID: 16117823 [PubMed - indexed for MEDLINE]

1: [Clin Chem Lab Med.](#) 1998 Apr;36(4):215-22.

Salivary cortisol--an alternative to serum cortisol determinations in dynamic function tests.

[Aardal-Eriksson E](#), [Karlberg BE](#), [Holm AC](#).

Department of Biomedicine and Surgery, Faculty of Health Sciences, Linköping University, Sweden.

Salivary cortisol was measured as an alternative to serum cortisol as a marker for adrenocortical function following insulin tolerance test, corticotropin-releasing-hormone stimulation and adreno-corticotrophic hormone stimulation. During insulin tolerance test and corticotropin-releasing-hormone stimulation adreno-corticotrophic hormone was also measured. The tests were performed on healthy control subjects as well as on patients under investigation for various disturbances in the hypothalamic-pituitary-adrenocortical axis (insulin tolerance test: 3 controls on two occasions and 14 patients; corticotropin-releasing-hormone stimulation: 4 controls and 18 patients; adreno-corticotrophic hormone stimulation: 6 controls and 10 patients). Five patients underwent both insulin tolerance test and corticotropin-releasing-hormone stimulation. Using criteria for adequate cortisol response in serum, the patients were classified as good or poor responders. In 42 of the 45 tests performed the same conclusion as to cortisol status was drawn when based on serum and salivary cortisol responses. In healthy subjects and good responders the mean cortisol relative increase was greater in saliva than in serum in all three tests ($p < 0.05$). Characteristic of the results for the insulin tolerance test was a significant initial mean decrease ($p < 0.05$), not found in serum, and the highest observed salivary cortisol value was delayed for at least 30 minutes compared to that in serum. Plasma adreno-corticotrophic hormone correlated significantly with the cortisol concentrations determined 15 minutes later in serum ($r = 0.54-0.64$) and in saliva ($r = 0.76-0.85$). The more pronounced cortisol response in saliva than in serum and its closer correlation with adreno-corticotrophic hormone offer advantages over serum cortisol, suggesting salivary cortisol measurement may be used as an alternative parameter in dynamic endocrine test.

PMID: 9638346 [PubMed - indexed for MEDLINE]

1: [Horm Res.](#) 2005;64(2):55-60. Epub 2005 Aug 9.

Adrenocortical response to ovine corticotropin-releasing hormone in young men: cortisol measurement in matched samples of saliva and plasma.

[Kumar AM](#), [Solano MP](#), [Fernandez JB](#), [Kumar M](#).

Department of Psychiatry and Behavioral Sciences, Division of Diabetes Research Institute, University of Miami Miller School of Medicine, FL 33101, USA. akumar@med.miami.edu

BACKGROUND: Assessment of hypothalamic-pituitary-adrenal (HPA) axis function in stress-related health problems in humans is frequently carried out as a dynamic test by measuring the profile of increment in adrenocortical hormone (ACTH) and/or cortisol level in plasma in response to corticotropin-releasing hormone (CRH) administration. However, obtaining multiple blood samples for this type of test is not only an invasive procedure but also problematic to use in individuals with constricted or damaged veins which collapse during the blood draw such as the injecting drug users (IDUs) and HIV-1-infected individuals. Salivary cortisol measurement presents a non-invasive alternate approach to evaluate HPA axis activity in different situations. In order to validate the efficacy of salivary cortisol measurement for a dynamic test in IDUs and HIV-1-infected individuals, the present study was carried out to evaluate the cortisol profile in matched samples of plasma and saliva in healthy young men in response to ovine CRH (oCRH) administration. METHODS: Cortisol levels were measured in matched samples of plasma and saliva of healthy young men at baseline and over a 90-min period after administration of a single low dose of oCRH (1 microg/kg). RESULTS: Salivary cortisol levels were found to follow the profile similar to that of plasma, increasing significantly at each time point after oCRH administration from their respective baseline values (all Sign tests, $p < 0.05$). The peak level of cortisol occurred at 30 min in both fluids. Although salivary cortisol concentration was a fraction of the total plasma cortisol levels at all time points, there was a significant correlation in the values between the two fluids at baseline ($r = 0.87$, $p < 0.02$) as well as at 90 min ($r = 0.70$, $p < 0.03$). CONCLUSION: The findings support the earlier studies and substantiate the efficacy of using salivary free cortisol measurement for assessment of dynamic function of pituitary-adrenal axis in healthy young men and its application in individuals such as IDUs and HIV-infected individuals who may have difficulty in donating multiple blood samples.

PMID: 16103684 [PubMed - indexed for MEDLINE]

Functional Adrenal Stress Profile

The Functional Adrenal Stress Profile assesses the levels of cortisol and of the sulfate form of DHEA: **DHEA-S**.

This profile assesses the body's ongoing level of adrenal response to both internal and external stressors. Chronic degenerative disease is an often insidious and debilitating stressor. Since adrenal exhaustion is implicated in all chronic degenerative disease, restoration of normal adrenal function is essential in the treatment and prevention of such disorder.

The Functional Adrenal Stress Profile is a salivary test requiring four saliva samples taken throughout the course of a patient's typical day which allows the cortisol circadian rhythm to be evaluated. Two of these samples (noon and afternoon) provide an average DHEA-S value.

This profile can identify stages I through III of adrenal exhaustion, which provides an accurate assessment of adrenal dysfunction.

The test results listed under Stages I, II, and III (stages of adrenal exhaustion) are not intended to be representative of all possible test results - however, they do provide important guidelines and effective protocols.

Results in Stage I are rarely seen since most people in Stage I generally have adequate reserves and they often feel well. These are not typical patients that are presenting with complaints related to adrenal exhaustion. However, patients in Stage I are often heading to Stage II and eventually Stage III, short of having excellent genetics and an optimal approach to diet, stress management, sleep, and exercise.

Clinical Note

The adrenal protocols listed in this guide do not take into consideration patients on thyroid, as improving adrenal function (augmenting DHEA and pregnenolone) can significantly improve thyroid function, thereby reducing the amount of thyroid medication necessary. Given this possibility it is suggested that any patient on thyroid should be closely monitored and lower dosages of pregnenolone and DHEA should be initially considered.

Stage I Adrenal Exhaustion

- **An Initial Increase in Cortisol Output**

- At least One Cortisol is High
- Total Cortisol Sum is High
- DHEA is Borderline Low, Low, or Normal

Distinguishing features:

- (↑) anterior pituitary output of ACTH
- (↑) adrenocortical stimulation
- (↑) cortisol output
- (↑) probability of pregnenolone steal
- (↑) probability of (↓) DHEA

Stage I Adrenal Exhaustion is defined as a prolonged, increased excitatory stimulus to the adrenals having resulted in a prolonged, increased cortisol output, usually with a corresponding prolonged **decrease in DHEA**.

In the hypothalamic-pituitary-adrenal control loop (HPA axis), an increase in ACTH output from the pituitary gland stimulates the adrenal glands. The level of cortisol is regulated through the HPA negative feedback. Continued demand for increased cortisol production necessitates ongoing ACTH release by the pituitary, but the adrenals can eventually experience difficulty in meeting the demand. This difficulty begins during the first stage of adrenal exhaustion.

Eventually, other pathways must compensate to facilitate the production of sufficient cortisol. One such compensation is often a **shunt or "steal" of pregnenolone**, which was discussed above.

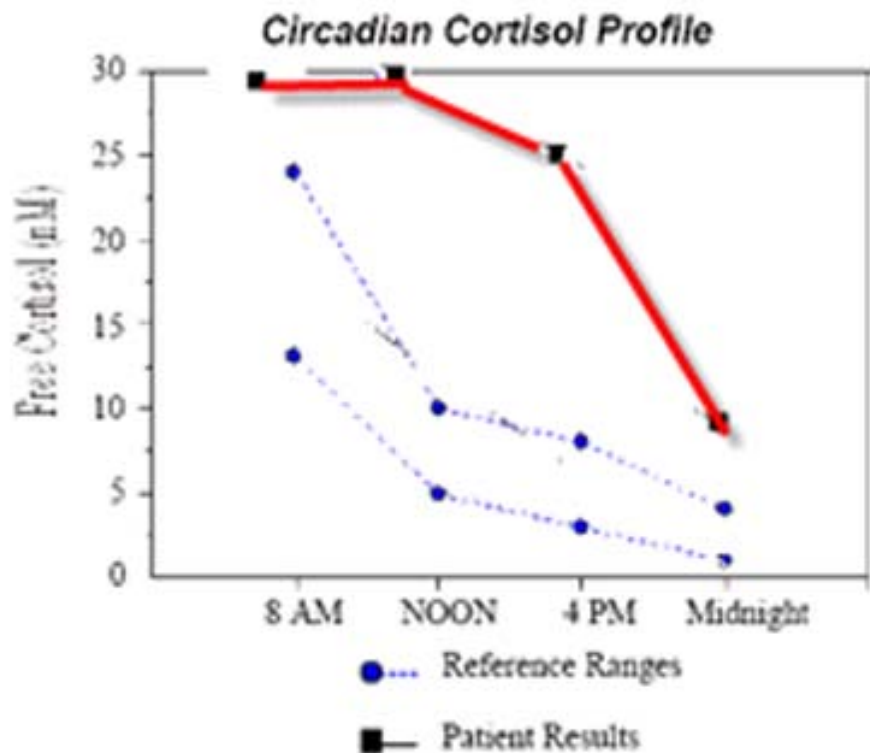
As we just learned, there is a decrease in DHEA and its metabolites, which include testosterone and the estrogens. Progesterone either remains normal or decreases, and cortisol increases. The overall cortisol increase in Stage I, therefore, is due to a combination of **increased cortisol output by the adrenals, and pregnenolone steal**.

ASI Adrenal Stress Index

TAP Free Cortisol Rhythm

07:00 - 08:00 AM	95	Elevated	13-24 nM
11:00 - Noon	45	Elevated	5-10 nM
04:00 - 05:00 PM	25	Elevated	3-8 nM
11:00 - Midnight	10	Elevated	1-4 nM

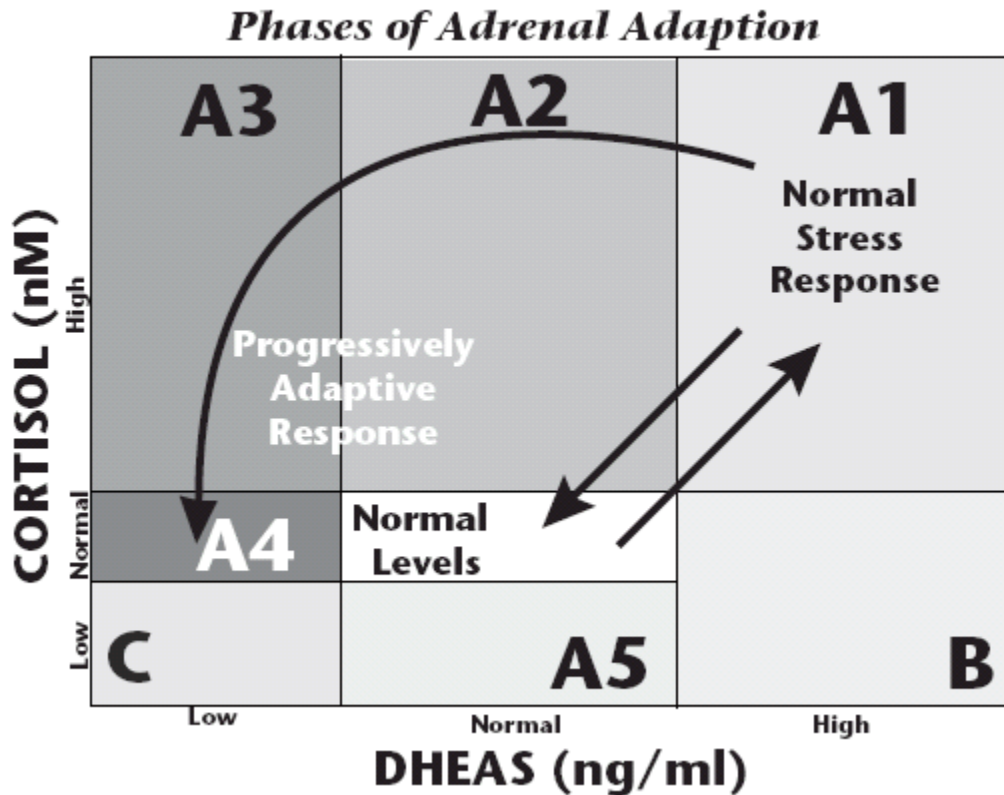
Cortisol Burden: **175** Elevated **23 - 42**



DHEA Dehydroepiandrosterone

Pooled Value 4 Normal Adults (M/F): 3-10 ng/ml

Phases of Adapatation



© Diagnos-techs

Patterns of Adaptive Responses

When forced to respond to continued, chronic stress the adrenal glands enter a compensated phase in which the production of the stress hormones is divergent. Because of the difference in response to ACTH, the production of DHEA falls as cortisol remains elevated. The process is shown graphically in Figure 3 where the initial stress response is labeled “A1”. The negative feedback of cortisol on the hypothalamus is lost as higher cortisol is required to shut down adrenal responses and bring ACTH into the normal range.

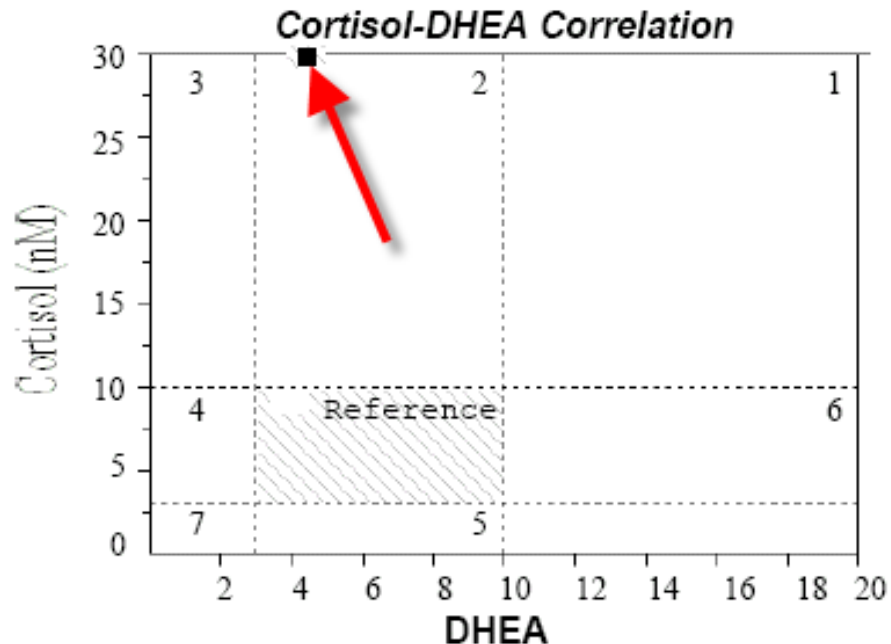
Calculating the Adrenal Adaptation and the Zone Placement

Take the sum total of the **noon and afternoon cortisols** and divide by 2. This calculation represents the vertical cortisol on the above graph. The DHEAS number represents the horizontal figure on the above graph.

Stress Responses of Cortisol and DHEA

Later phases of compensated response may go through the progression from “A2” to “A5”. The progression has been called ‘stress fixation’. Output of DHEA falls from high to normal to low followed by the same progression for cortisol. If the stress is prolonged,

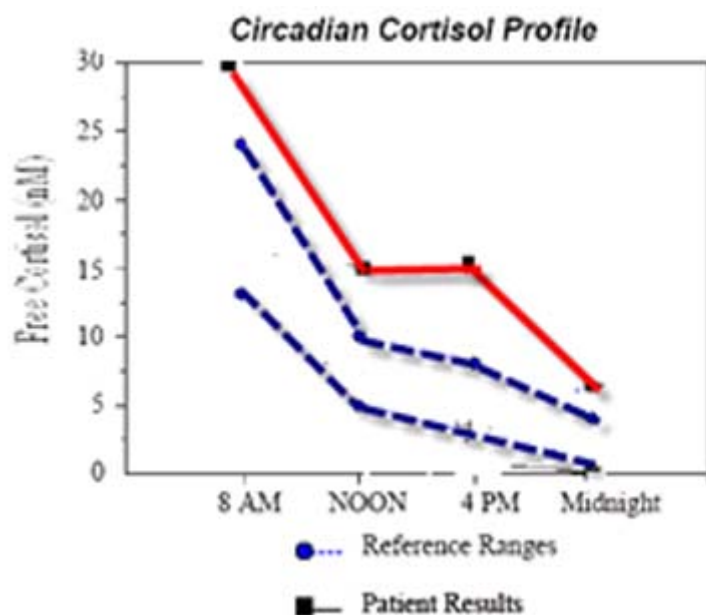
the production of both hormones falls into the sector labeled “C”. Individuals affected with Addison’s disease where the adrenals are unable to produce stress hormones have values that fall into the “C” sector. The rare finding of elevated DHEA with normal or low cortisol (Type “B”) is genetically determined and these individuals should avoid high stress occupations.



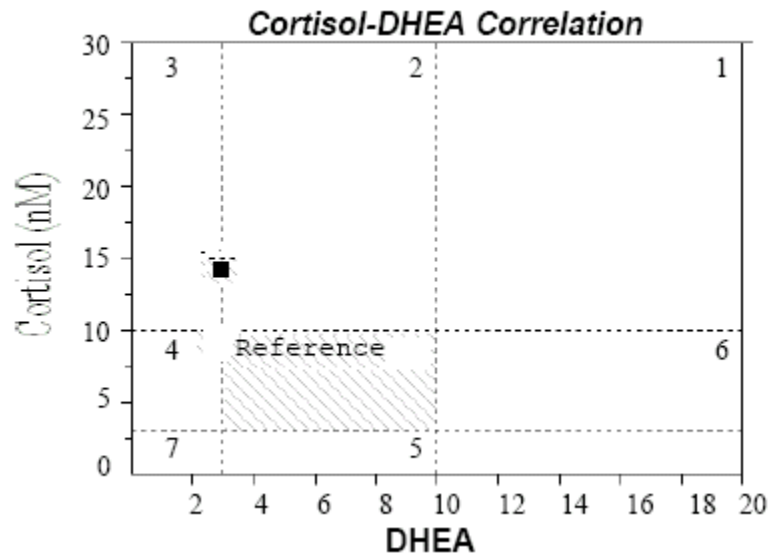
CORTISOL-DHEA CORRELATION SPECTRUM

1. Adapted to stress.
2. Adapted with DHEA slump.
3. Maladapted Phase I.
4. Maladapted Phase II.
5. Non-adapted, Low Reserves
6. High DHEA.
7. Adrenal Fatigue.

Test	Description	Result	Ref Values
ASI	Adrenal Stress Index		
TAP	Free Cortisol Rhythm		
	07:00 - 08:00 AM	30 Elevated	13-24 nM
	11:00 - Noon	14 Elevated	5-10 nM
	04:00 - 05:00 PM	15 Elevated	3-8 nM
	11:00 - Midnight	9 Elevated	1-4 nM
		68 Elevated	23 - 42



DHEA **Dehydroepiandrosterone**
 Pooled Value **3** Normal Adults (M/F): 3-10 ng/ml



CORTISOL-DHEA CORRELATION SPECTRUM

1. Adapted to stress.
2. Adapted with DHEA slump.
3. Maladapted Phase I.
4. Maladapted Phase II.
5. Non-adapted, Low Reserves
6. High DHEA.
7. Adrenal Fatigue.

RON GRISANTI, DC
 4200 E NORTH ST
 SUITE 18
 GREENVILLE SC 29615
 USA Tel: 864-292-0226 Fax: 1-864-268-7022

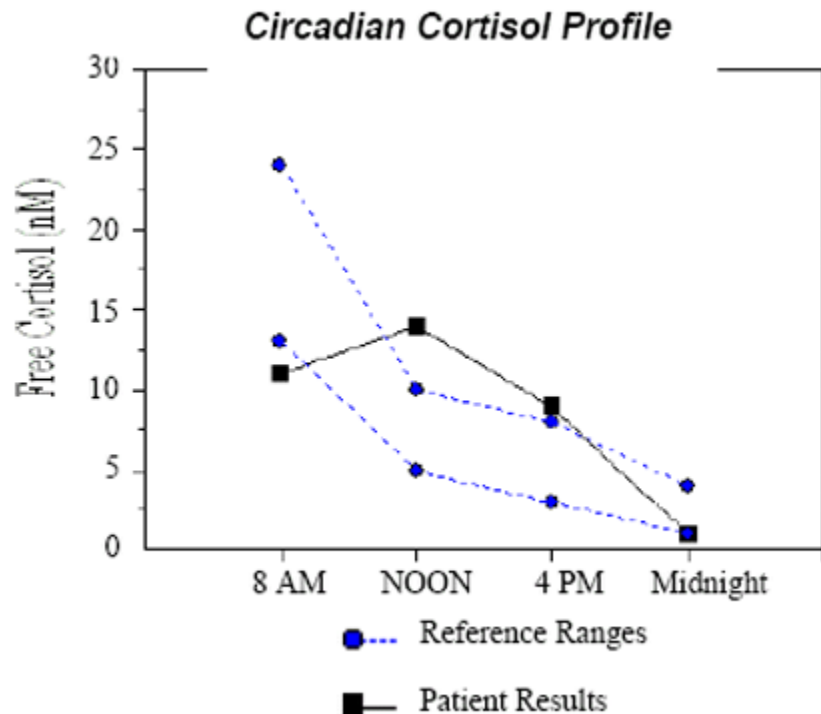
Test	Description	Result	Ref Values
------	-------------	--------	------------

ASI Adrenal Stress Index

TAP Free Cortisol Rhythm

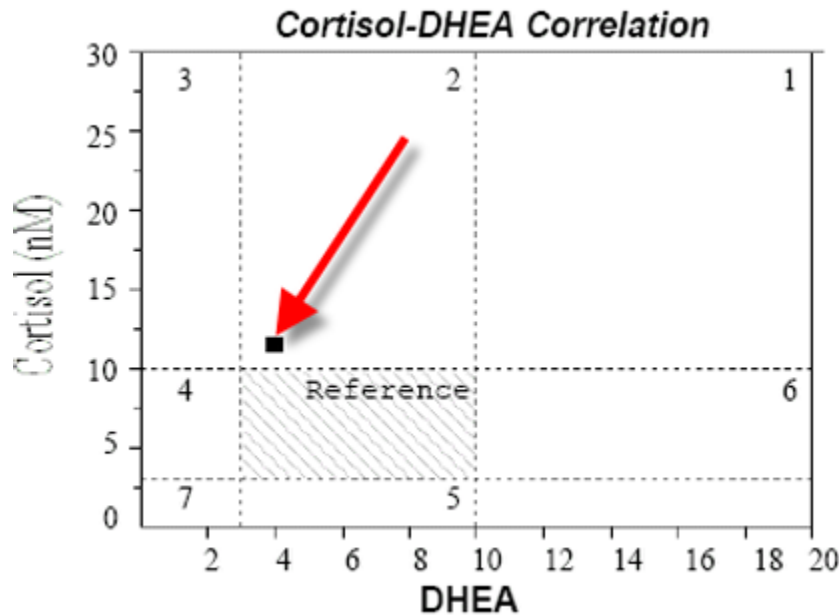
07:00 - 08:00 AM	11	Depressed	13-24 nM
11:00 - Noon	14	Elevated	5-10 nM
04:00 - 05:00 PM	9	Elevated	3-8 nM
11:00 - Midnight	1	Normal	1-4 nM

Cortisol Burden: 35 23 - 42



DHEA Dehydroepiandrosterone

Pooled Value 4 Normal Adults (M/F): 3-10 ng/ml



1. Adapted to stress.

2. Adapted with DHEA slump.

3. Maladapted Phase I.

4. Maladapted Phase II.

5. Non-adapted, Low Reserves

6. High DHEA.

7. Adrenal Fatigue.

Stage II Adrenal Exhaustion

- **The Transition from Increased to Decreased Cortisol Output**

- AM, Noon or Afternoon Cortisols are Low or Borderline Low

- Total Cortisol Sum is Normal

- DHEA is Borderline Low or Low

Distinguishing features:

- (↑) anterior pituitary output of ACTH
- (↑) adrenocortical stimulation
- normal total cortisol output
- low or borderline-low morning, noon, or afternoon cortisol level

- normal nighttime cortisol level
- (↑) probability of pregnenolone steal
- (↑) probability of (↓) DHEA

Stage II Adrenal Exhaustion is a transitional phase and can be very misleading. Don't be fooled thinking that a Stage II represent a normal finding. It actually signifies a continuing decline in cortisol output from levels above normal to those below normal, although ACTH stimulation remains high or even increases.

There is a gradual change from increased to decreased cortisol output due to a decreasing response of the adrenal glands to protracted ACTH stimulation.

Any one or more of the morning, noon, or afternoon cortisol values is low or borderline-low, but the nighttime cortisol level is usually normal. The decreasing cortisol output is a marker of mid-stage adrenal exhaustion.

In this transitory stage the sum of the four cortisol levels is nevertheless normal which again can be misleading.

Pregnenolone steal from the DHEA/sex hormone pathway to the progesterone/cortisol pathway can assist in maintaining normal overall cortisol levels at the continued expense of DHEA. DHEA usually remains low or borderline-low.

Adrenal Stress Index

Free Cortisol Rhythm

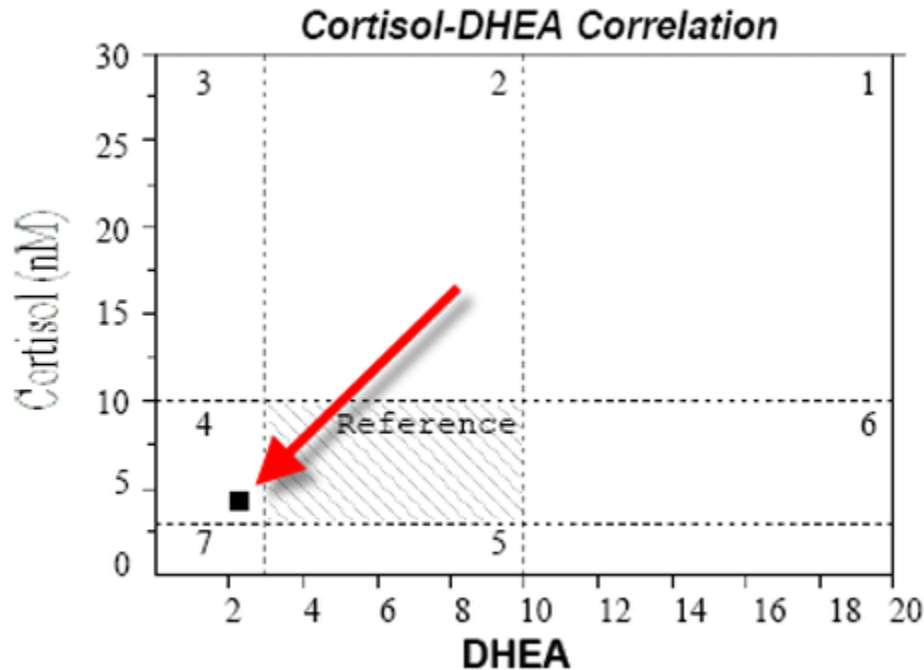
07:00 - 08:00 AM	16 Normal	13-24 nM
11:00 - Noon	4 Depressed	5-10 nM
04:00 - 05:00 PM	2 Depressed	3-8 nM
11:00 - Midnight	1 Normal	1-4 nM

Cortisol Burden: **23** **23 - 42**

DHEA Dehydroepiandrosterone
Pooled Value

2.2 Depressed

Adults (M/F): 3-10 ng/ml



CORTISOL-DHEA CORRELATION SPECTRUM

1. Adapted to stress.
2. Adapted with DHEA slump.
3. Maladapted Phase I.
4. Maladapted Phase II.
5. Non-adapted, Low Reserves.
6. High DHEA.
7. Adrenal Fatigue.

Stage III Adrenal Exhaustion

• The Advanced Stage with Decreased Cortisol Output

- ✚ Most Cortisols are Low or Borderline Low
- ✚ Total is Cortisol Low
- ✚ DHEA is Borderline Low or Low

Distinguishing features:

- (↑) anterior pituitary output of ACTH
- (↑) adrenocortical stimulation

- (↓) total cortisol output
- (↑) probability of (↓) nighttime cortisol level
- (↑) probability of pregnenolone steal
- (↑) probability of (↓) DHEA

Stage III is the terminal stage of adrenal exhaustion. It is marked by the failure of the adrenals to produce enough cortisol to reach even normal levels in response to continued, increased ACTH stimulation.

The sum of the four cortisol levels is below normal, and DHEA is usually low or borderline-low.

Endocrine and autonomic pathways, through endogenous and/or exogenous stress, have been conditioned by a complex of stimuli to respond beyond normal physiological ranges. This conditioning ultimately results in adrenal gland inability to produce the amount of cortisol demanded by the degree of stimulation. The result is a hypothalamic-pituitary-adrenal axis "crash," in which essential neuroendocrine feedback loops are endogenously unable to return the system to homeostasis.

In such a case there is often a **decreased nighttime cortisol, which is a marker of late Stage III adrenal exhaustion.**

A wide variety of seemingly unrelated symptoms usually appears; a situation which reflects the global nature of the dysfunction. Severe imbalances in other hormone systems are to be expected. Subclinical disorders are common, indicating the insidiousness of advanced adrenal exhaustion. Adrenal failure is a natural sequela, and cardiovascular failure is a high probability.

Clinical Note

Low DHEA is a normal finding in children **below the age of 14** and DHEA augmentation is not recommended

Clinical Note:

Licorice will not be effective in cortisol augmentation when **morning cortisol is < 5nM**. It may be necessary to augment with 15 mgs of Hydrocortisone.

Clinical Note:

Pregnenolone augmentation is necessary when the **cortisol burden is very depressed <23 or >85**

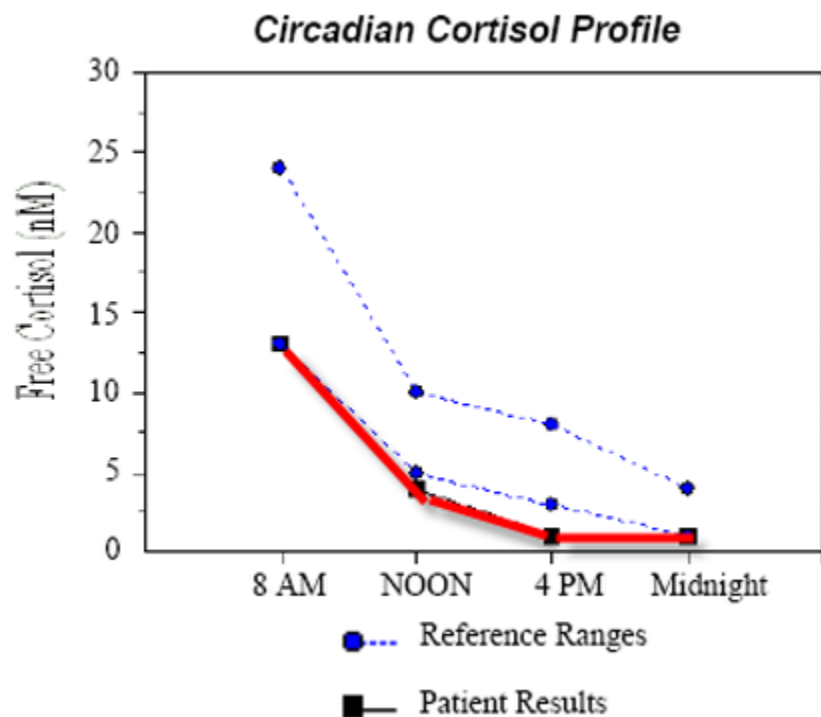
Clinical Note:

Cortisol augmentation is **contraindicated** in diabetic or pre-diabetic patients.

John 70 years old

RON GRISANTI, DC
4200 E NORTH ST
SUITE 18
GREENVILLE SC 29615
USA Tel: 864-292-0226 Fax: 1-864-268-7022

Test	Description	Result	Ref Values
ASI	<u>Adrenal Stress Index</u>		
TAP	Free Cortisol Rhythm		
	07:00 - 08:00 AM	13 Normal	13-24 nM
	11:00 - Noon	4 Depressed	5-10 nM
	04:00 - 05:00 PM	<1* Depressed	3-8 nM
	11:00 - Midnight	1 Normal	1-4 nM
	Cortisol Burden:	19	23 - 42



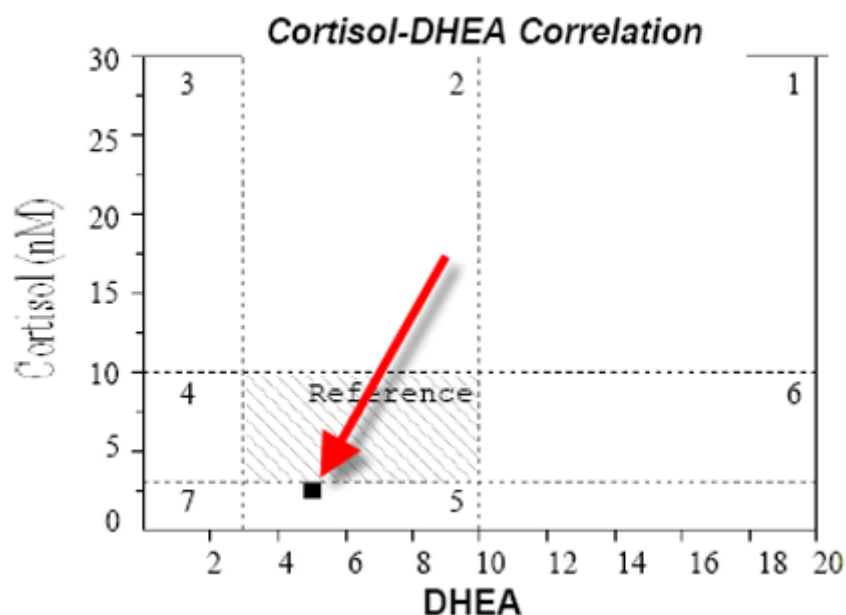
DHEA Dehydroepiandrosterone

Pooled Value

5

Normal

Adults (M/F): 3-10 ng/ml



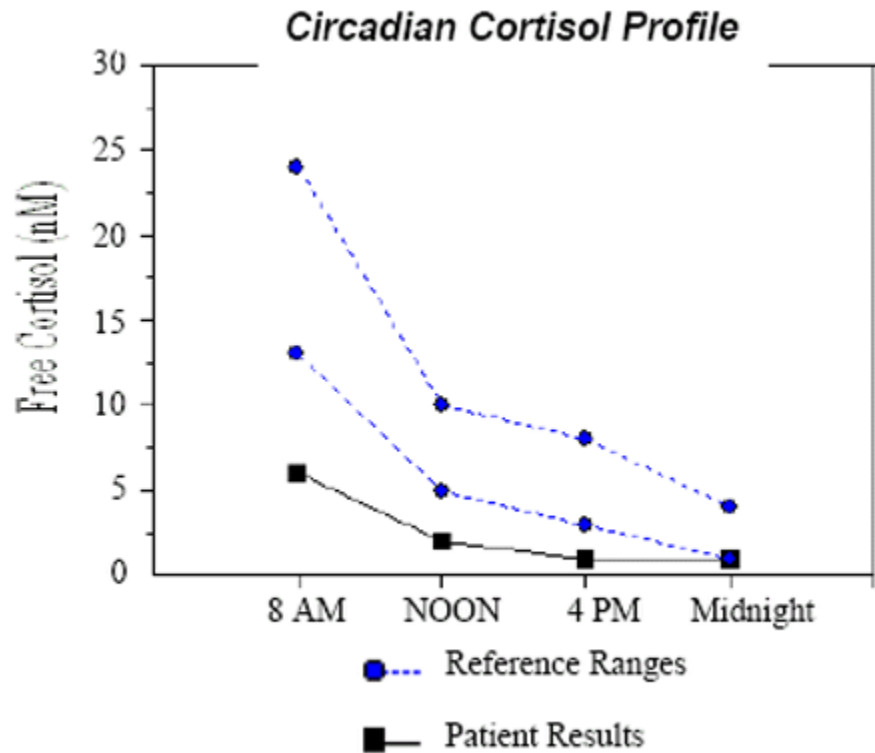
CORTISOL-DHEA CORRELATION SPECTRUM

1. Adapted to stress.
2. Adapted with DHEA slump.
3. Maladapted Phase I.
4. Maladapted Phase II.
- 5. Non-adapted, Low Reserves.**
6. High DHEA.
7. Adrenal Fatigue.

Lindsey 20 years old female

RON GRISANTI, DC
4200 E NORTH ST
SUITE 18
GREENVILLE SC 29615
USA Tel: 864-292-0226 Fax: 1-864-268-7022

Test	Description	Result	Ref Values
ASI	<u>Adrenal Stress Index</u>		
TAP	Free Cortisol Rhythm		
	07:00 - 08:00 AM	6 Depressed	13-24 nM
	11:00 - Noon	2 Depressed	5-10 nM
	04:00 - 05:00 PM	<1* Depressed	3-8 nM
	11:00 - Midnight	<1 Depressed	1-4 nM
	Cortisol Burden:	10	23 - 42



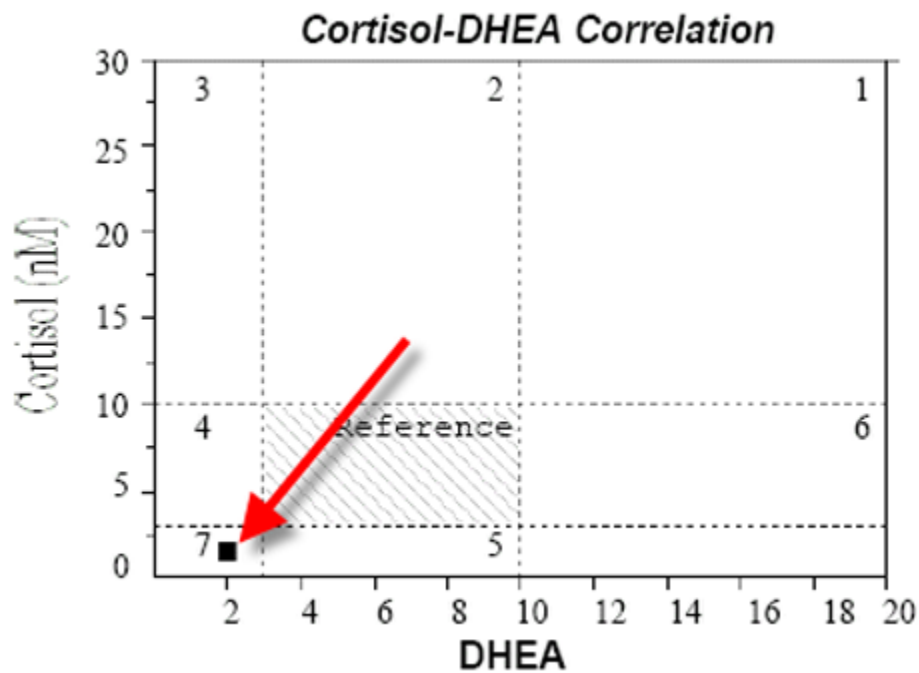
DHEA Dehydroepiandrosterone

Pooled Value

2

Depressed DHEA

Adults (M/F): 3-10 ng/ml



CORTISOL-DHEA CORRELATION SPECTRUM

1. Adapted to stress.
2. Adapted with DHEA slump.
3. Maladapted Phase I.
4. Maladapted Phase II.
5. Non-adapted, Low Reserves
6. High DHEA.
- 7. Adrenal Fatigue.**

Adrenal/DHEA Restoration

<u>High Cortisol:DHEA Ratio</u>	<u>Low Cortisol:DHEA Ratio</u>
<ul style="list-style-type: none">■ Pregnenolone■ DHEA■ “Support adrenals”■ Seriphos	<ul style="list-style-type: none">■ Licorice extract■ “Support adrenals”■ May need prescription cortisol■ Lifestyle changes

Credit is contributed to the following labs for their advancement in the field of functional medicine:

Diagnos-Techs, Inc.

Clinical and Research Laboratory

6620 S. 192nd Place, Bldg. J.

Kent, WA 98032

1-800-878-3787

<http://www.diagnostechs.com>

BioHealth Diagnostics

2929 Canon Street

San Diego, CA 92106

1- 800-570-2000

www.biodia.com