

HPA-D: DUTCH Test II - Part 2

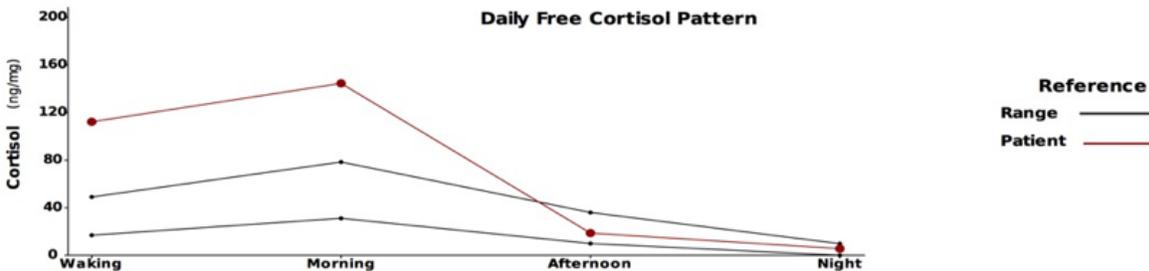
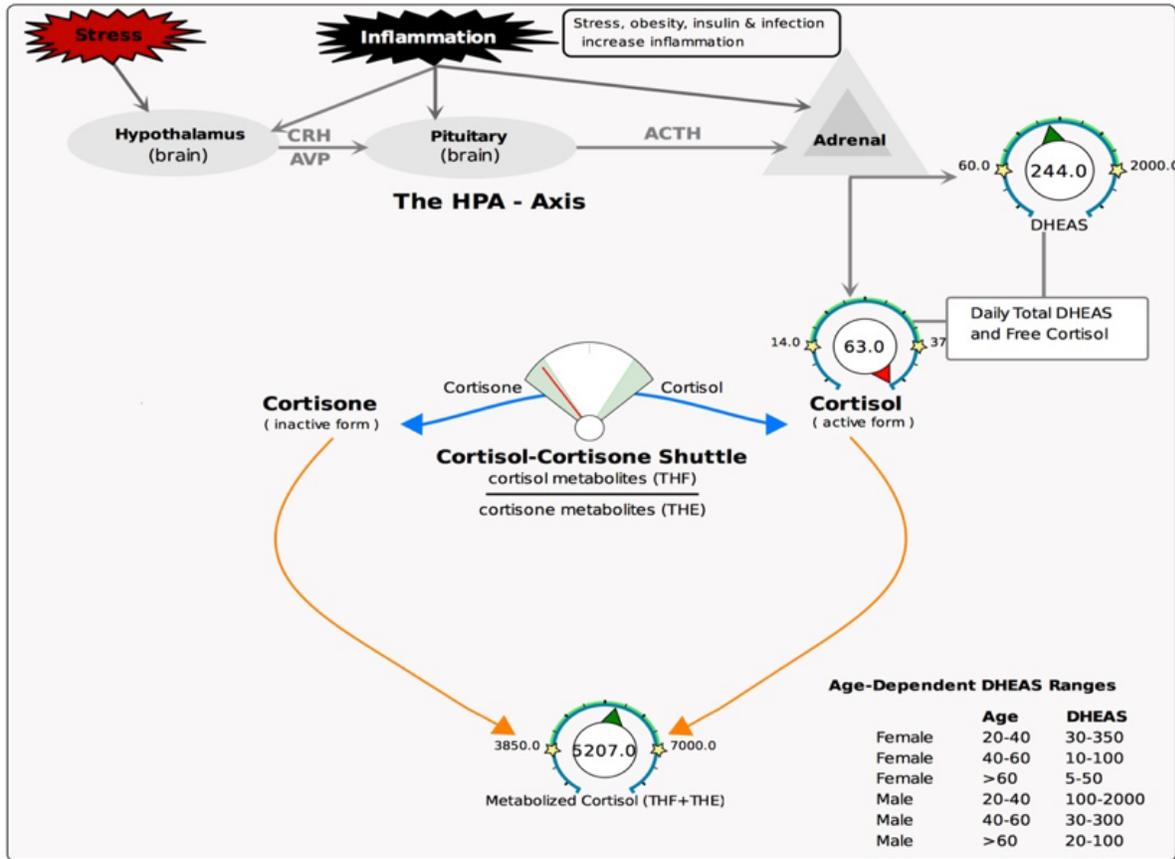
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Low/high melatonin

Let's talk a little bit about low and high melatonin. Earlier in the presentation, I explained that 6-OH melatonin sulfate is a good representation of the night's production of melatonin, but it can't be used to monitor therapy, so keep that in mind when you're interpreting results for melatonin.

Melatonin plays a crucial role in regulating body temperature, the sleep-wake cycle, female reproductive hormones, and cardiovascular function. Low melatonin has been observed in anxiety, stress, depression, seasonal affective disorder, sleep disorders, delayed sleep phase syndrome, immunological disorders, cardiovascular disease, and cancer. High melatonin without supplementation has been observed in certain neuroinflammatory conditions.

Ordering physician: Chris Kresser		DOB: 1978-03-30	Collection Times:		
		Gender: Male	2015-05-17 06:30PM		
			2015-05-17 10:00PM		
			2015-05-18 03:30AM		
			2015-05-18 06:00AM		
			2015-05-18 08:00AM		
Category	Test		Result	Units	Normal Range
Creatinine					
	Creatinine A (Waking)	Within range	0.78	mg/ml	0.3 - 3
	Creatinine B (Morning)	Within range	1.09	mg/ml	0.3 - 3
	Creatinine C (Afternoon)	Within range	1.0	mg/ml	0.3 - 3
	Creatinine D (Night)	Within range	0.9	mg/ml	0.3 - 3
Daily Free Cortisol and Cortisone					
	Cortisol A (Waking)	Above range	112.2	ng/mg	16.9 - 49
	Cortisol B (Morning)	Above range	144.5	ng/mg	31.1 - 78.4
	Cortisol C (Afternoon)	Within range	18.7	ng/mg	9.9 - 36
	Cortisol D (Night)	Within range	5.6	ng/mg	0 - 9.8
	Cortisone A (Waking)	Above range	159.9	ng/mg	55 - 118.4
	Cortisone B (Morning)	Above range	209.2	ng/mg	100.8 - 163.8
	Cortisone C (Afternoon)	Low end of range	37.8	ng/mg	37.3 - 115.2
	Cortisone D (Night)	Within range	23.3	ng/mg	0 - 49.2
	Cortisol-24hr (AUC)	Above range	63.0	ug	14 - 37
	Cortisone-24hr (AUC)	Above range	97.0	ug	57 - 90
Cortisol Metabolites and DHEAS					
	b-Tetrahydrocortisol (b-THF)	Low end of range	1504.0	ng/mg	1330 - 2330
	a-Tetrahydrocortisol (a-THF)	Within range	363.0	ng/mg	220 - 720
	b-Tetrahydrocortisone (b-THE)	Within range	3340.0	ng/mg	2100 - 4000
	Metabolized Cortisol (THF+THE)	Within range	5207.0	ng/mg	3850 - 7000
	DHEAS	Low end of range	244.0	ng/mg	60 - 2000
Melatonin (*measured as 6-OH-Melatonin-Sulfate)					
	Melatonin* (Waking)	Below range	1.6	ng/mg	10 - 50



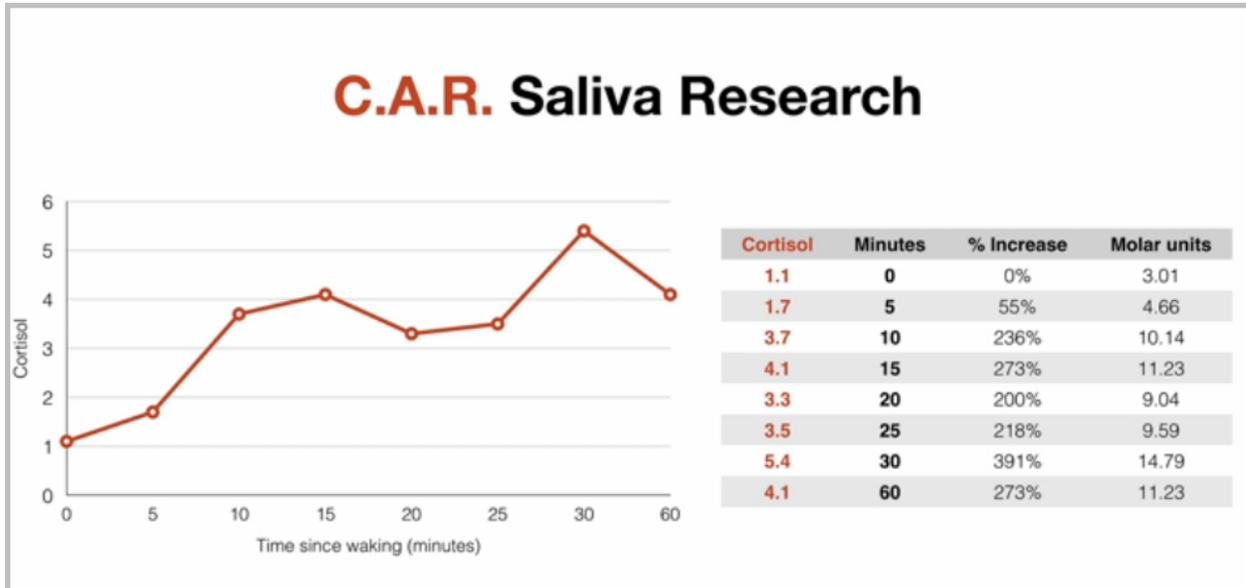
Here is a 37-year-old male with sleep issues as his primary complaint. He routinely wakes at 3 to 4 a.m. and can't fall back to sleep. Check out his melatonin. It is 1.6 in a range of 10 to 50. When you see low melatonin like this, you always want to look at cortisol because, as we've discussed, cortisol opposes melatonin, and melatonin opposes cortisol. His nighttime cortisol is not elevated, but look at his overnight reading. It's more than two times the upper limit. He is making a lot of cortisol throughout the night, and that is suppressing his melatonin production, and it explains why he wakes up at 3 to 4 a.m. and can't get back to sleep.

Ordering physician:		DOB:1952-02-27		Collection Times:	
Chris Kresser		Gender: Female		2015-02-07 05:00PM 2015-02-07 08:15PM 2015-02-08 01:00AM 2015-02-08 05:30AM 2015-02-08 07:30AM	
Category	Test	Result	Units	Normal Range	
Creatinine					
	Creatinine A (Overnight)	Below range	0.36	mg/ml	0.5 - 3
	Creatinine B (Morning)	Within range	1.48	mg/ml	0.5 - 3
	Creatinine C (Afternoon)	Below range	0.23	mg/ml	0.5 - 3
	Creatinine D (Night)	Below range	0.39	mg/ml	0.5 - 3
Daily Free Cortisol and Cortisone					
	Cortisol A	Low end of range	11.0	ng/mg	10.8 - 39.3
	Cortisol B	Low end of range	27.3	ng/mg	24.5 - 87
	Cortisol C	Below range	5.9	ng/mg	6.8 - 20.8
	Cortisol D	Within range	1.9	ng/mg	0 - 7.6
	Cortisone A	Low end of range	53.8	ng/mg	47.2 - 142.9
	Cortisone B	Low end of range	118.6	ng/mg	103.7 - 267.5
	Cortisone C	Below range	29.8	ng/mg	46.5 - 135.5
	Cortisone D	Within range	19.9	ng/mg	0 - 52.3
	Cortisol-24hr (AUC)	Below range	9.0	ug	11 - 31
	Cortisone-24hr (AUC)	Below range	47.0	ug	49 - 131
Cortisol Metabolites and DHEAS					
	a-Tetrahydrocortisol (a-THF)	Within range	189.0	ng/mg	134 - 281
	b-Tetrahydrocortisol (b-THF)	Within range	1186.0	ng/mg	783 - 1317
	b-Tetrahydrocortisone (b-THE)	Low end of range	1723.0	ng/mg	1490 - 2795
	Metabolized Cortisol (THF+THE)	Within range	3098.0	ng/mg	2412 - 4504
	DHEAS	Low end of range	32.0	ng/mg	23 - 252
Melatonin (*measured as 6-OH-Melatonin-Sulfate)					
	Melatonin* (Overnight)	Above range	69.369	ng/mg	10 - 50

This patient is a 64-year-old female with a four-year history of Lyme disease and attendant problems with chronic fatigue, neurological dysfunction, cognitive issues, anxiety, and other problems. Her melatonin is only slightly high. This is more typical when melatonin is high due to endogenous production rather than supplementation. Research suggests that one possible cause of elevated melatonin is inflammation in the brain and central nervous system. This would be consistent with her Lyme presentation because Lyme often affects the brain and central nervous system. It causes neuroinflammation. The astrocytes and glial cells have been proven to produce melatonin. When inflammation in the central nervous system is present, the brain produces higher levels of melatonin to protect the neurons and the microglia from oxidative stress. It explains why melatonin is being studied to slow progression of neurodegenerative disorders like Alzheimer's disease.

Ordering physician: Chris Kresser		DOB: 1969-01-08 Gender: Female		Collection Times: 2015-02-01 10:00PM 2015-02-02 06:30AM 2015-02-02 07:30PM 2015-02-02 08:30AM	
Category	Test		Result	Units	Normal Range
Creatinine					
	Creatinine A (Overnight)	Within range	1.06	mg/ml	0.5 - 3
	Creatinine B (Morning)	Within range	1.51	mg/ml	0.5 - 3
	Creatinine C (Afternoon)	Below range	0.35	mg/ml	0.5 - 3
	Creatinine D (Night)	Within range	0.78	mg/ml	0.5 - 3
Daily Free Cortisol and Cortisone					
	Cortisol A	Below range	7.2	ng/mg	10.8 - 39.3
	Cortisol B	Below range	13.0	ng/mg	24.5 - 87
	Cortisol C	Below range	3.5	ng/mg	6.8 - 20.8
	Cortisol D	Within range	5.9	ng/mg	0 - 7.6
	Cortisone A	Below range	40.2	ng/mg	47.2 - 142.9
	Cortisone B	Below range	61.0	ng/mg	103.7 - 267.5
	Cortisone C	Below range	44.7	ng/mg	46.5 - 135.5
	Cortisone D	Within range	27.2	ng/mg	0 - 52.3
	Cortisol-24hr (AUC)	Below range	6.0	ug	11 - 31
	Cortisone-24hr (AUC)	Below range	42.0	ug	49 - 131
Cortisol Metabolites and DHEAS					
	b-Tetrahydrocortisol (b-THF)	Within range	1165.0	ng/mg	783 - 1317
	a-Tetrahydrocortisol (a-THF)	Within range	196.0	ng/mg	134 - 281
	b-Tetrahydrocortisone (b-THE)	Within range	2026.0	ng/mg	1490 - 2795
	Metabolized Cortisol (THF+THE)	Within range	3386.0	ng/mg	2412 - 4504
	DHEAS	Low end of range	43.0	ng/mg	23 - 252
Melatonin (*measured as 6-OH-Melatonin-Sulfate)					
	Melatonin* (Overnight)	Above range	3158.420	ng/mg	10 - 50

This is what melatonin levels look like when the patient is supplementing. You can see the range is 10 to 50, and this patient's level is 3,158. That would be pretty alarming if you weren't aware of the effects that melatonin supplementation has on 6-hydroxymelatonin sulfate. This is more than 60 times higher than the upper end of the reference range, and it is orders of magnitude higher than what you would see with neuroinflammatory conditions. As I mentioned, it is not pathological.



Before we finish this presentation, I want to briefly discuss using saliva testing to measure the cortisol awakening response. Combining this with the DUTCH test is probably the best overall view of the HPA axis and the stress response that we can get with currently available testing methods. Unfortunately, no saliva testing lab at the time of this recording offers a CAR test, but you can just order a typical adrenal stress index from any lab, and you can kind of hack the results yourself.

So upon rising, you would have the patient rinse his or her mouth. They can keep a glass of water near their bed, then immediately collect saliva for two to three minutes, and then collect again at 30, 45, and 60 minutes. It is best to drink a little fluid in between the samples but not eat. When you get the results, you'll have to ignore their report because the report is predicated on taking samples at morning, late morning, afternoon, and midnight, but you can use the guidelines here on this slide. For a healthy CAR, you should see an increase in cortisol between 350 and 600 percent in the first 30 minutes. The tables and chart on this slide depict a cortisol awakening response test that Mark Newman, the director of Precision Analytical, did on himself using these guidelines. As you can see, he hit 391 percent at 30 minutes, which is right in the range that I just gave you.

Note that some studies on the cortisol awakening response use molar units. Others use nanograms per milliliter, but either way, the percent increase should still fall between 350 and 600.

Cortisol Awakening Response (CAR) indications

Elevated

Job-related stress

High perceived stress

Depression

Anxiety

Faster M.S. progression

Acute coronary syndrome

Decreased

Depression

Schizophrenia

PTSD

Psychosocial burnout

Chronic fatigue syndrome

Type 2 diabetes

Here is a partial list of indications for an altered cortisol awakening response. A high CAR is related to job stress, high perceived stress, depression, anxiety, faster MS progression, and acute coronary syndrome. A decreased cortisol awakening response has been observed in depression, schizophrenia, PTSD, psychosocial burnout, chronic fatigue syndrome, and type 2 diabetes. There are certain conditions such as depression and metabolic disease that are characterized by both blunted or decreased and elevated CAR in the scientific literature.

Pattern	Indication
High free cortisol (with normal or high total)	Perceived stress, inflammation, circadian disruption, Cushing's
High nighttime/evening free cortisol	Depression, sleep deprivation, PTSD, cognitive impairment, circadian disruption, type 2 diabetes, Cushing's syndrome/disease
Disrupted diurnal rhythm only	Fatigue, sleep disturbance, stress/HPA axis activation, non-pathological
Low free cortisol (with low or normal total)	Metabolic syndrome, fibromyalgia, CFS, chronic pain, cardiometabolic disease, mood disorders, autoimmune disease, cancer, Addison's disease, corticosteroid/opioid use
High free cortisol with low total	Hypothyroidism, licorice supplementation, inflammation, normal/nonpathological
Low free cortisol with high total	Obesity, insulin resistance, hyperthyroidism, chronic stress, glucocorticoid use, chronic fatigue syndrome
High DHEA	PCOS, acute stress, obesity, benzodiazepenes (e.g. Xanax), antidepressants (e.g. Wellbutrin), A.D.D. meds
Low DHEA	Stress, aging, rapid weight loss, opioids, glucocorticoids, birth control, HRT/estrogens, antipsychotics, diabetes meds
High cortisol:cortisone ratio	Hypothyroidism, inflammation, visceral obesity, high insulin, excess sodium, and licorice
Low cortisol:cortisone ratio	Hyperthyroidism, hGH, estradiol, good sleep, ketoconazole, magnolia, scutellaria, zizyphus, and testosterone
Low melatonin	Anxiety, stress, depression, seasonal affective disorder, sleep disorders, immunological disorders, cardiovascular disease, cancer
High melatonin	Neuroinflammatory conditions

Okay, so here is a summary of what we've discussed. We're going to have a handout for you with this table and each of the patterns and the indications. So high free cortisol with normal or high total cortisol is observed in perceived stress, inflammation, circadian disruption, and Cushing's disease. High nighttime or evening free cortisol is observed in depression, sleep deprivation, PTSD, cognitive impairment, circadian disruption, type 2 diabetes, and Cushing's syndrome and disease. If you see only a disrupted diurnal cortisol rhythm, that is observed in fatigue, sleep disturbance, stress and HPA axis activation, and certain nonpathological states. If you see low free cortisol with low or normal total or metabolized cortisol, that can be observed in metabolic syndrome, fibromyalgia, chronic fatigue syndrome, chronic pain, cardiometabolic disease, mood disorders, autoimmune disease, cancer, Addison's disease, and corticosteroid and opioid use.

For the discordant patterns, we have high free cortisol with low total or metabolized cortisol in hypothyroidism, licorice supplementation, inflammation, and in some cases normal or nonpathological states. Low free cortisol with high total or metabolized cortisol is observed in obesity, insulin resistance, hyperthyroidism, chronic stress, glucocorticoid use, and chronic fatigue syndrome.

High DHEA production is seen in PCOS, acute stress, obesity, benzodiazepines, antidepressants, and some ADD meds, whereas low DHEA is seen in stress, aging, rapid weight loss, opioids, glucocorticoids, birth control, HRT or estrogen use, antipsychotics, and some diabetes meds.

Now for the cortisol-to-cortisone ratio, a high ratio is seen in hypothyroidism, inflammation, visceral obesity, high insulin levels, excess sodium, and licorice use, whereas a low ratio is seen in

hyperthyroidism, human growth hormone use, estradiol, good sleep, ketoconazole, and adaptogens such as magnolia, scutellaria, and ziziphus, and hormones such as testosterone.

Low melatonin is seen in anxiety, stress, depression, seasonal affective disorder, sleep disorders, immunological disorders, cardiovascular disease, and cancer. High melatonin is observed in neuroinflammatory conditions.

Okay, that's it for now. I'll see you next time.