dutchplus
COMPLETE WITH CORTISOL AWAKENING RESPONSE

PRECISION ANALYTICAL INC.
SIMPLY · BETTER · TESTING

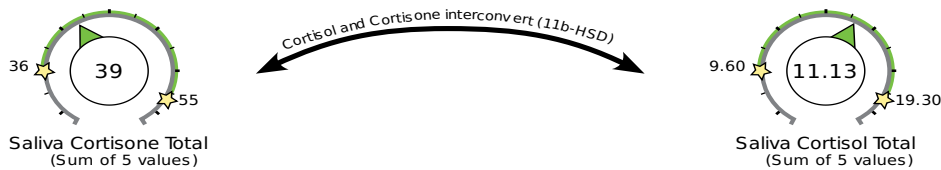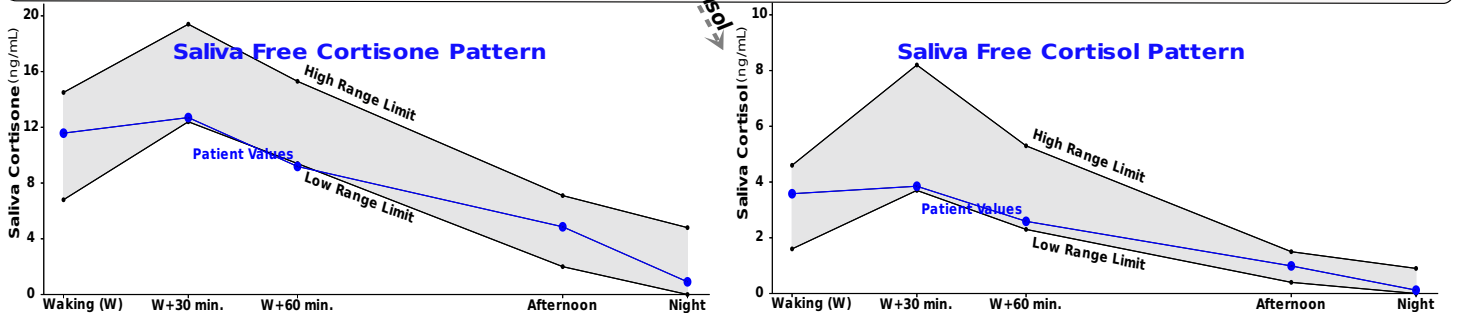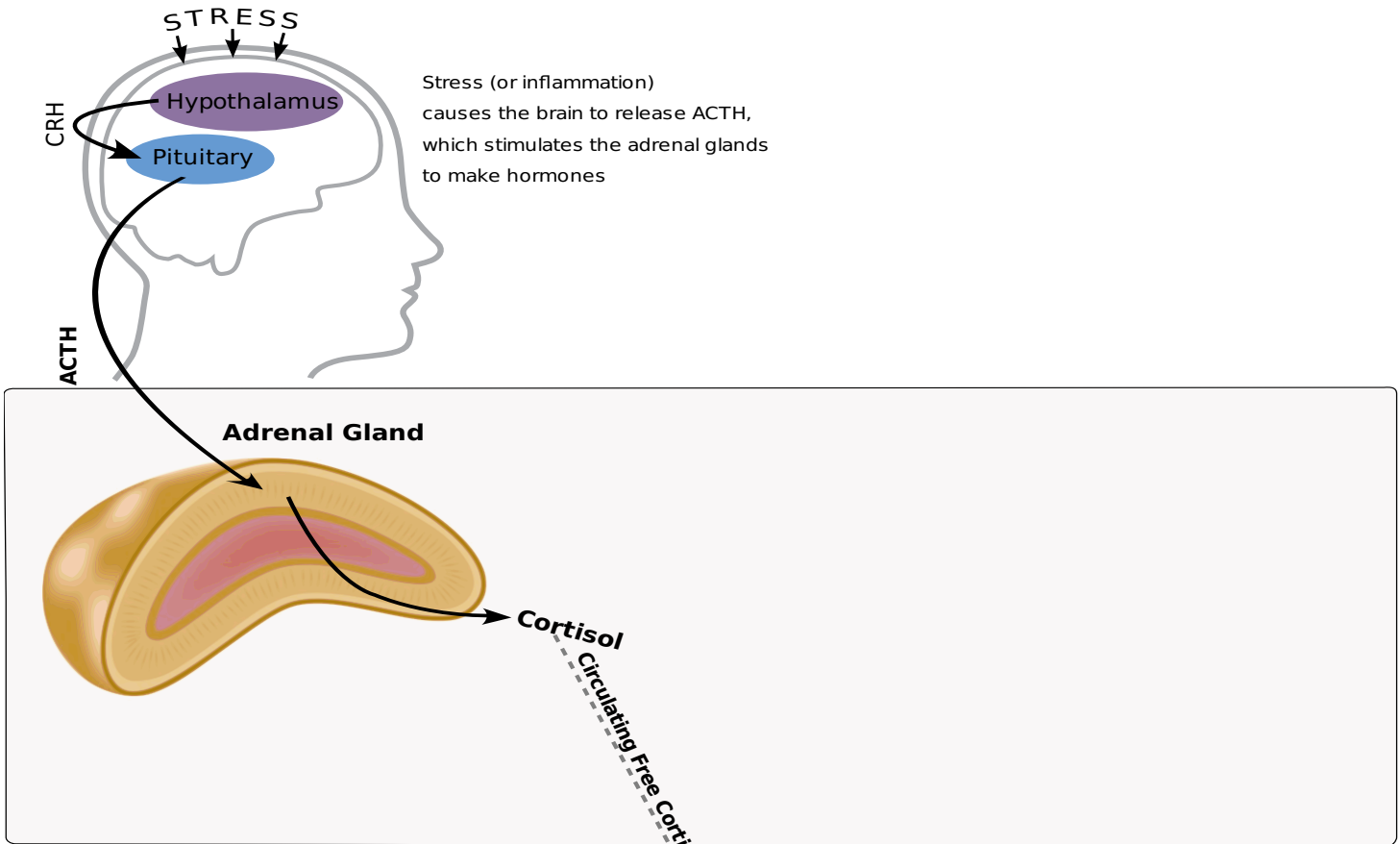## *Cortisol Awakening Response*

Last Menstrual Period:

Ordering Physician:
Precision Analytical

DOB: 1953-10-10
Age: 63
Gender: Female

Collection Times:
2017-08-09 06:01AM (S)
2017-08-09 06:31AM (S)
2017-08-09 07:01AM (S)
2017-08-09 05:01PM (S)
2017-08-09 10:01PM (S)
2017-08-09 01:30AM (S*)

Category	Test		Result	Units	Normal Range
Free Cortisol and Cortisone (Saliva)					
	Saliva Cortisol - Waking (W)	Within range	3.58	ng/mL	1.6 - 4.6
	Saliva Cortisol - W+30 min.	Low end of range	3.85	ng/mL	3.7 - 8.2
	Saliva Cortisol - W+60 min.	Low end of range	2.59	ng/mL	2.3 - 5.3
	Saliva Cortisol - Afternoon	Within range	0.99	ng/mL	0.4 - 1.5
	Saliva Cortisol - Night	Low end of range	0.12	ng/mL	0 - 0.9
	Saliva Cortisone - Waking (W)	Within range	11.58	ng/mL	6.8 - 14.5
	Saliva Cortisone - W+30 min.	Low end of range	12.7	ng/mL	12.4 - 19.4
	Saliva Cortisone - W+60 min.	Below range	9.19	ng/mL	9.4 - 15.3
	Saliva Cortisone - Afternoon	Within range	4.86	ng/mL	2 - 7.1
	Saliva Cortisone - Night	Low end of range	0.91	ng/mL	0 - 4.8
	Saliva Cortisol Total	Low end of range	11.13	ng/mL	9.6 - 19.3
	Saliva Cortisone Total	Low end of range	39.24	ng/mL	36 - 55
Additional Cortisol and Cortisone (Saliva)					
	* Saliva Cortisol - Insomnia	Above range	2.1	ng/mL	0 - 0.9
	* Saliva Cortisone - Insomnia	Above range	10.4	ng/mL	0 - 4.8

STRESS

Hypothalamus

CRH

Pituitary

Stress (or inflammation)
causes the brain to release ACTH,
which stimulates the adrenal glands
to make hormones

ACTH

Adrenal Gland

Cortisol

Circulating Free Cortisol

Saliva Free Cortisone Pattern

Saliva Cortisone (ng/mL)

High Range Limit

Patient Values

Low Range Limit

| Waking (W) | W+30 min. | W+60 min. | Afternoon | Night |

Saliva Free Cortisol Pattern

Saliva Cortisol (ng/mL)

High Range Limit

Patient Values

Low Range Limit

| Waking (W) | W+30 min. | W+60 min. | Afternoon | Night |

Cortisol and Cortisone interconvert (11b-HSD)

36 **39** 55
Saliva Cortisone Total
(Sum of 5 values)

9.60 **11.13** 19.30
Saliva Cortisol Total
(Sum of 5 values)

- The patient submitted an Insomnia salivary sample. The cortisol result for this sample was 2.10ng/mL (expected range 0-0.9) The cortisone result for this sample was 10.4 ng/mL (expected range 0-4.8)

The Cortisol Awakening Response (CAR) is the rise in salivary cortisol between the waking sample and the sample collected 30 (as well as 60) minutes later. This "awakening response" is essentially a "mini stress test" and is a useful measurement in addition to the overall up-and-down (diurnal) pattern of free cortisol throughout the day. **This patient shows a waking cortisol of 3.58 and an increase to 3.85 after 30.0 minutes. This is an increase of 0.27ng/mL or 7.5%.** Expected increases differ depending on the methods used. Preliminary research shows that 50-160% or 1.5-4.0ng/mL increases are common with samples collected 30 minutes after waking. These guidelines are considered research only.
This patient shows a salivary cortisol of 2.59 measured 60 minutes after waking. Generally this result is a little higher than the waking sample but is not in this case. To date, data suggests that expected results may be 0-70% higher, and this guideline is considered for research only.

Precision Analytical (Raymond Grimsbo, Lab Director)
3138 Rivergate Street #301C
McMinnville, OR 97128

Female Sample Report
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Provider Notes

DUTCH Adrenal

The HPA-Axis refers to the communication and interaction between the hypothalamus (H) and pituitary (P) in the brain down to the adrenal glands (A) that sit on top of your kidneys. When a physical or psychological stressor occurs, the hypothalamus tells the pituitary to make ACTH, a hormone. ACTH stimulates the adrenal glands to make the stress hormone, cortisol and to a lesser extent DHEA and DHEA-S. Normally, the HPA-axis production follows a daily pattern in which cortisol rises rather rapidly in the first 10-30 minutes after waking (this is the C.A.R.) in order to help with energy, then gradually decreases throughout the day so that it is low at night for sleep. The cycle starts over the next morning. Abnormally high activity occurs in Cushing's Disease where the HPA-axis is hyper-stimulated causing cortisol to be elevated all day. The opposite is known as Addison's Disease, where cortisol is abnormally low because it is not made appropriately in response to ACTH's stimulation. These two conditions are somewhat rare. Examples of more common conditions related to less severely abnormal cortisol levels include fatigue, depression, insomnia, fibromyalgia, anxiety, inflammation and more.

Only a fraction of cortisol is "free" and bioactive. This fraction of cortisol is very important, but levels of metabolized cortisol best represent overall production of cortisol therefore both should be taken into account to correctly assess adrenal function.

When evaluating cortisol levels, it is important to assess the following:

- **The overall up-and-down pattern of free cortisol throughout the day, looking for low and high levels:**
Abnormal results should be considered along with related symptoms.
- **The sum of the free cortisol as an expression of the overall tissue cortisol exposure:**
This total of five free cortisol measurements is the best way to assess the total of free cortisol throughout the day, but do be aware that it is heavily weighted towards the morning production since three of five measurements are made within the first hour of the day.
- **The Cortisol Awakening Response (CAR):**
The unique feature of the DUTCH Plus is the inclusion of the CAR assessment. The response to waking adds one more piece to HPA-axis function. In some cases overall levels of free cortisol may be normal, but the response to stress may be under or overactive. Reasons for a lower CAR might include: an underactive HPA Axis, excessive psychological burnout, seasonal affective disorder (SAD), sleep apnea or poor sleep in general, PTSD, and "chronic fatigue" patients. An elevated CAR can be a result of an over-reactive HPA axis, ongoing job-related stress (anticipatory stress for the day), glycemic dysregulation, pain (ie. waking with painful joints or a migraine), and general depression (not SAD). Scientific literature points to the magnitude of the morning cortisol increase as being connected to HPA-axis health whether the overall production of cortisol is low, normal or high.

- The patient submitted an Insomnia salivary sample. The cortisol result for this sample was 2.10ng/mL. The cortisone result was 10.4 ng/mL. Ranges can be found in the table on the last page.

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Reference Range Determination (last updated 12.20.2018)

We aim to make the reference ranges for our DUTCH tests as clinically appropriate and useful as possible. This includes the testing of thousands of healthy individuals and combing through the data to exclude those that are not considered "healthy" or "normal" with respect to a particular hormone. As an example, we only use a premenopausal woman's data for estrogen range determination if the associated progesterone result is within the luteal range (days 19-21 when progesterone should be at its peak). We exclude women on birth control or with any conditions that may be related to estrogen production. Over time the database of results for reference ranges has grown quite large. This has allowed us to refine some of the ranges to optimize for clinical utility. The manner in which a metabolite's range is determined can be different depending on the nature of the metabolite. For example, it would not make clinical sense to tell a patient they are deficient in the carcinogenic estrogen metabolite, 4-OH-E1 therefore the lower range limit for this metabolite is set to zero for both men and women. Modestly elevated testosterone is associated with unwanted symptoms in women more so than in men, so the high range limit is set at the 80th percentile in women and the 90th percentile for men. Note: the 90th percentile is defined as a result higher than 90% (9 out of 10) of a healthy population.

Classic reference ranges for disease determination are usually calculated by determining the average value and adding and subtracting two standard deviations from the average, which defines 95% of the population as being "normal." When testing cortisol, for example, these types of two standard deviation ranges are effective for determining if a patient might have Addison's (very low cortisol) or Cushing's (very high cortisol) Disease. Our ranges are set more tightly to be optimally used for Functional Medicine practices.

Below you will find a description of the range for each test:

Female Reference Ranges (Updated 12.20.2018)								
	Low%	High%	Low	High		Low%	High%	Low	High
b-Pregnanediol	20%	90%	600	2000	Saliva Cortisol Waking (W)	20%	90%	1.6	4.6
a-Pregnanediol	20%	90%	200	740	Saliva Cortisol (W+30 min.)	20%	90%	3.7	8.2
Estrone (E1)	20%	80%	12	26	Saliva Cortisol (W+60 min.)	20%	90%	2.3	5.3
Estradiol (E2)	20%	80%	1.8	4.5	Saliva Cortisol (Afternoon)	20%	90%	0.4	1.5
Estriol (E3)	20%	80%	5	18	Saliva Cortisol (Night)	0	95%	0	0.9
2-OH-E1	20%	80%	5.1	13.1	Saliva Cortisol (2-3 am)	0	90%	0	0.9
4-OH-E1	0	80%	0	1.8	Saliva Cortisone Waking (W)	20%	90%	6.8	14.5
16-OH-E1	20%	80%	0.7	2.6	Saliva Cortisone (W+30 min.)	20%	90%	12.4	19.4
2-Methoxy-E1	20%	80%	2.5	6.5	Saliva Cortisone (W+60 min.)	20%	90%	9.4	15.3
2-OH-E2	0	80%	0	1.2	Saliva Cortisone Afternoon	20%	90%	2	7.1
4-OH-E2	20%	80%	0.15	0.5	Saliva Cortisone Night	0	95%	0	4.8
2-Methoxy-E2	20%	80%	0.3	0.7	Saliva Cortisone (2-3 am)	0	95%	0	4.8
DHEA-S	20%	90%	20	750	Melatonin (6-OHMS)	20%	90%	10	85
Androsterone	20%	80%	200	1650	8-OHdG	0	90%	0	5.2
Etiocholanolone	20%	80%	200	1000	Methylmalonate	0	90%	0	2.2
Testosterone	20%	80%	2.3	14	Xanthurenate	0	90%	0	1.4
5a-DHT	20%	80%	0	6.6	Kynurenate	0	90%	0	7.3
5a-Androstanediol	20%	80%	12	30	Pyroglutamate	10%	90%	32	60
5b-Androstanediol	20%	80%	20	75	Homovanillate	10%	95%	4	13
Epi-Testosterone	20%	80%	2.3	14	Vanilmandelate	10%	95%	2.4	6.4
a-THF	20%	90%	75	370					
b-THF	20%	90%	1050	2500	**Calculated Values**				
b-THE	20%	90%	1550	3800	Total DHEA Production	20%	80%	500	3000
% = population percentile: Example - a high limit of 90% means results higher than 90% of the women tested for the reference range will be designated as "high."					Total Estrogens	20%	80%	35	70
					Metabolized Cortisol	20%	90%	2750	6500
					Saliva Cortisol Total	20%	90%	9.6	19.3
					Saliva Cortisone Total	20%	90%	36	55

Provider Notes:

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