



Accession # 00268797
 Female Sample Report
 123 A Street
 Sometown , CA 90266



Cortisol Awakening Response

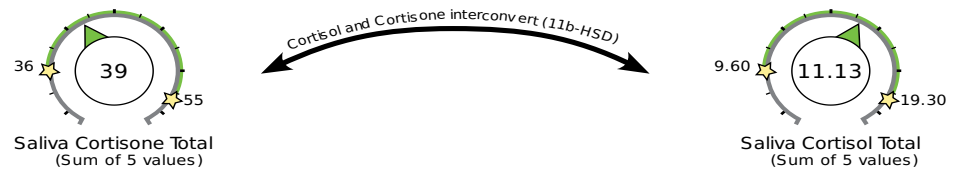
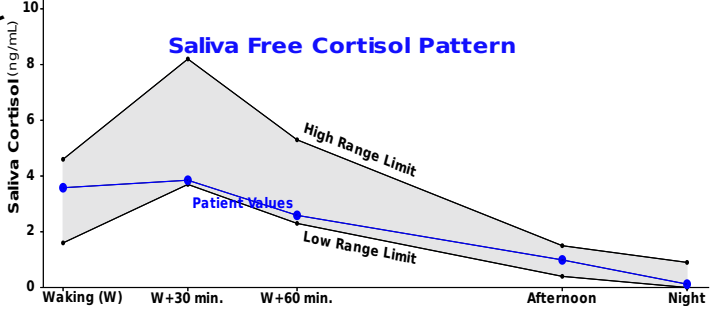
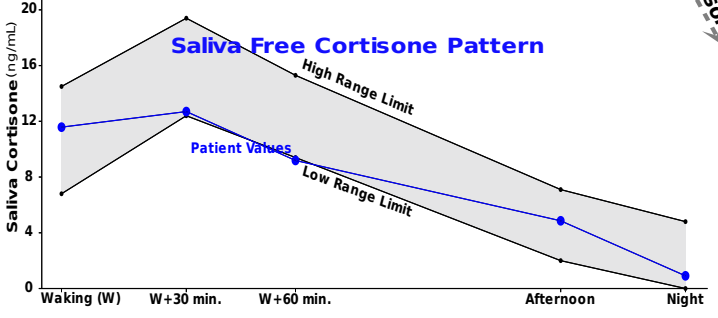
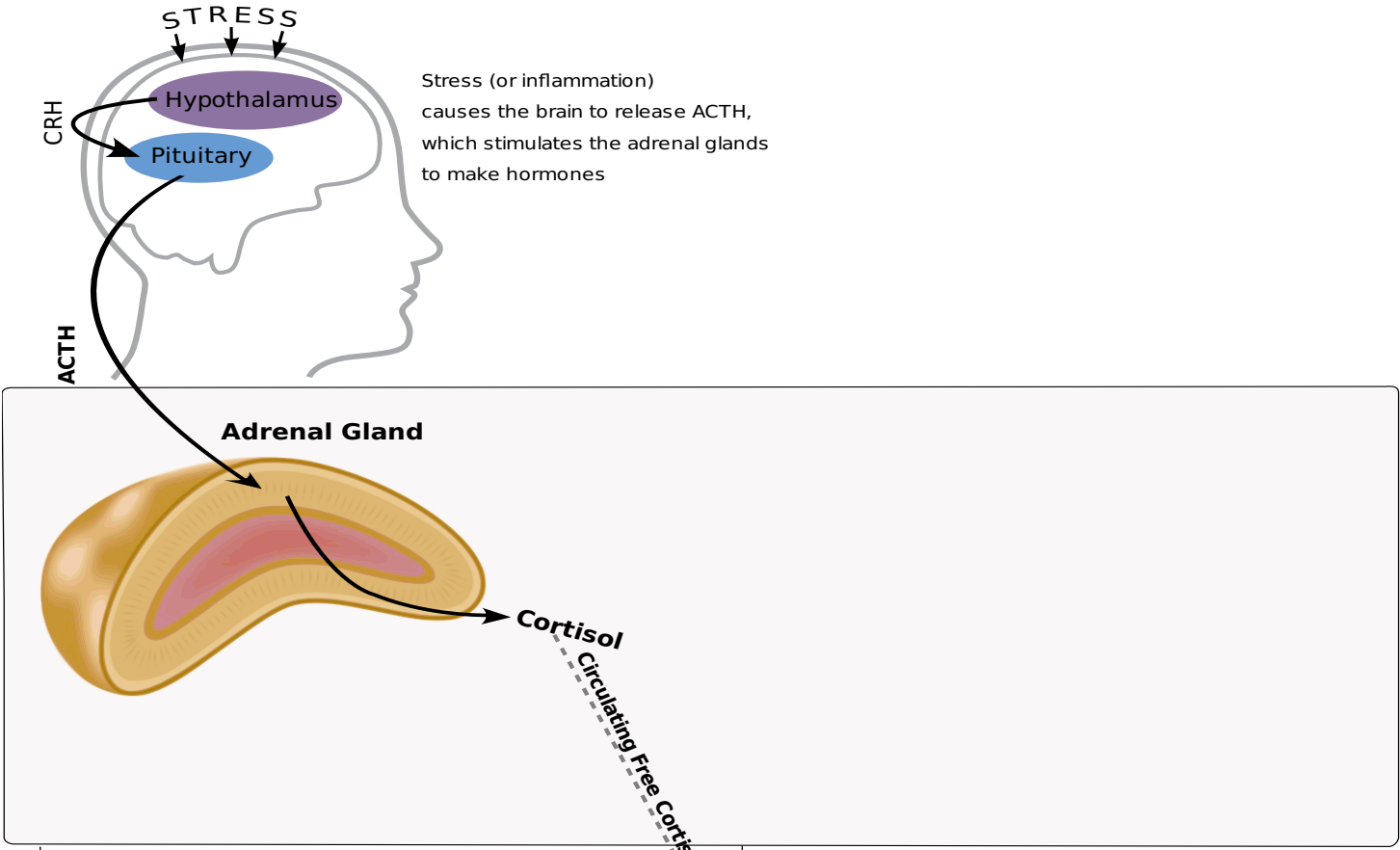
Last Menstrual Period:

Ordering Provider:
 Precision Analytical

DOB: 1992-01-04
Age: 25
Sex: 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 | Within 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 | Within 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 |



- 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.**

Clinical Support Overview

Alert comments:

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 cortisol is needed in the body, the hypothalamus releases cortisol releasing hormone (CRH) and the pituitary responds by releasing adrenocorticotrophic releasing Hormone (ACTH), which is the signal to the adrenal gland to release cortisol, DHEA and DHEA-s. It is these adrenal hormones that are assessed on the DUTCH test to understand the patient's HPA axis.

The cortisol awakening response is a complex interaction between the HPA axis, the hippocampus, and other brain structures. Cortisol normally surges right after waking leading to the day's highest levels of cortisol. This surge is considered by researchers to be separate from the regular circadian rhythm (the smooth transition from lower cortisol at night to modestly higher cortisol in the morning) and to reflect the person's anticipation of stress during the day, strong reaction to morning's first light, some psychosocial factors such as depression or anxiety and the patient's metabolic state. The waking surge in cortisol helps with energy, focus, morning blood sugar and immune regulation.

As the day progresses, ACTH declines and subsequent cortisol decreases throughout the day, so it is low at night for sleep. This cycle starts over the next morning.

Free cortisol provides negative feedback to CRH & ACTH. When free cortisol is too low, ACTH will surge. ACTH will also surge when a physical or psychological stressor occurs.

Only a small fraction of cortisol is "free" and bioactive. The "free" cortisol is what the person feels in terms of energy and focus, and it is also what feeds back to the hypothalamus and pituitary gland for ACTH and cortisol regulation. The free cortisol daily pattern is very useful for understanding cortisol and its interaction with the patient's symptoms throughout the day. However, because only a fraction of the cortisol is bioactive, when considering treatments that affect the whole HPA axis, including DHEA, it is essential to measure metabolized cortisol.

In urine, we can measure both the total metabolized cortisol (THF) and total metabolized cortisone (THE) excreted throughout the day. These two components better represent the total cortisol production from the adrenal glands than the free cortisol alone. Outside of the HPA axis, metabolism of cortisol occurs with the help of thyroid hormone in the liver. A significant amount of cortisol is also metabolized in adipose tissue.

To best determine total adrenal production of cortisol throughout the day it is important to measure both metabolized cortisol and free cortisol.

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:**

The patient is instructed to collect on a "typical" day because cortisol, as an acute response hormone, can vary from day to day if activities are very different. Abnormal results should be considered along with the patient's symptoms and any unusual occurrences of the day

- **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.

Reference Range Determination (last updated 02.25.2025)

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 02.25.2025) | | | | | | | | | |
|--|------|-------|------|-------|------------------------------|------|-------|------|------|
| | 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 | 3.1 | Saliva Cortisone Afternoon | 20% | 90% | 2 | 7.1 |
| 4-OH-E2 | 0 | 80% | 0 | 0.52 | Saliva Cortisone Night | 0 | 95% | 0 | 4.8 |
| 2-16-ratio | 20% | 80% | 2.69 | 11.83 | Saliva Cortisone (2-3 am) | 0 | 95% | 0 | 4.8 |
| 2-4-ratio | 20% | 80% | 5.4 | 12.62 | Melatonin (6-OHMS) | 20% | 90% | 10 | 85 |
| 2Me-2OH-ratio | 20% | 80% | 0.39 | 0.67 | 8-OHdG | 0 | 90% | 0 | 5.2 |
| DHEA-S | 20% | 90% | 20 | 750 | Methylmalonate | 0 | 90% | 0 | 2.5 |
| Androsterone | 20% | 80% | 200 | 1650 | Xanthurenate | 0 | 90% | 0.12 | 1.2 |
| Etiocolanalone | 20% | 80% | 200 | 1000 | Kynurenate | 0 | 90% | 0.8 | 4.5 |
| Testosterone | 20% | 80% | 2.3 | 14 | b-Hydroxyisovalerate | 0 | 90% | 0 | 12.5 |
| 5a-DHT | 0 | 80% | 0 | 6.6 | Pyroglutamate | 10% | 90% | 28 | 58 |
| 5a-Androstenediol | 20% | 80% | 6 | 30 | Indican | 0 | 90% | 0 | 100 |
| 5b-Androstenediol | 20% | 80% | 12 | 75 | Homovanillate | 10% | 95% | 3 | 11 |
| Epi-Testosterone | 20% | 80% | 2.3 | 14 | Vanilmandelate | 10% | 95% | 2.2 | 5.5 |
| a-THF | 20% | 90% | 75 | 370 | Quinolate | 0 | 90% | 0 | 9.6 |
| b-THF | 20% | 90% | 1050 | 2500 | | | | | |
| b-THE | 20% | 90% | 1550 | 3800 | | | | | |
| | | | | | Calculated Values | | | | |
| | | | | | Total DHEA Production | 20% | 80% | 500 | 3000 |
| | | | | | 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 |
| % = 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." | | | | | | | | | |