

# HPA-D DUTCH Test Part 1 Review

Precision Analytical offers several different panels:

## DUTCH COMPREHENSIVE HORMONE PROFILE

- Covers free cortisol, free cortisone, cortisol metabolites, DHEA, androgens such as etiocholanolone and androsterone, melatonin, and then sex hormones such as progesterone, estrogen, estrogen metabolites, testosterone, and 5 $\alpha$ -DHT.

## ADVANCED ADRENAL PANEL:

- Provides the information on the adrenal hormones only: free cortisol, cortisone, cortisol metabolites, and DHEA sulfate.
- Doesn't contain melatonin or androsterone/etiocholanolone.

## DUTCH COLLECTION INSTRUCTIONS

### DUTCH complete instructions

### When to collect

## TIMING OF DUTCH TESTING

	<b>Timing</b> (Adrenal only)	<b>Timing</b> (Comprehensive)
<b>Male</b>	Doesn't matter	Doesn't matter
<b>Female</b> (normal cycle)	Doesn't matter	Between days 19-22
<b>Female</b> (longer cycle)	Doesn't matter	Add # of days beyond 28 day cycle
<b>Female</b> (shorter cycle)	Doesn't matter	Subtract # of days less than 28 day cycle
<b>Female</b> (no cycle)	Doesn't matter	Watch irregular cycle collection video*

### Sample collection videos.

If cycles are irregular, or the patient has amenorrhea, direct them to watch the irregular cycle collection video in the video library at dutchtest.com for suggestions on collection, but the basic idea is to aim for the time in the cycle where progesterone levels are the highest and estrogen levels are relatively high, which would be midway through the luteal phase in cycling women. They can take their basal body temperature to determine when they're ovulating and then sample six to seven days after that.

A more foolproof way is to measure luteinizing hormone, LH levels, with an ovulation predictor kit that can be purchased from a drugstore, and when LH shoots up, that indicates ovulation, and then they would just count six to seven days after that.

- Testing should be done on a day that is average in terms of stress levels. If they work during the week, they should do the testing on a weekday, not the weekend.
- Avoid caffeine on the day of the test
- No vigorous exercise right before or during the test.

Collection takes place over two days. See the DUTCH instruction handout for specifics.

If they're taking hormones, they need to follow the instructions (see links above) in the test kit carefully.

- Skip all oral hormones except progesterone on the day of the test, and skip pregnenolone if they're taking it for two days.
- No need to skip any hormone creams or gels while taking that test.
- Hormones taken at night and oral progesterone, as usual, should be taken after sample #2.
- On collection day two, they would take their morning hormones and meds after sample #4. They wouldn't take any morning hormones before sample #3 or sample #4.
- Glucocorticoids will affect the results, so you have a couple of options:
  1. See what the results look like when they are on the glucocorticoids.
  2. If they can manage without taking them for a couple of days, have them stop a couple of days ahead of time, and then do the test.

#### **Note on melatonin**

1. If the patient is dependent on melatonin for sleep and skipping it leads to poor sleep, that will mess up cortisol results, and I think accurate cortisol results are more important. In this case, they can keep taking it. Just know that the melatonin levels you see on the test results won't be accurate.
2. Alternatively, if they can stop taking melatonin for one to two nights, instruct them to do so in order to get an accurate test reading.

#### **MARKERS IN THE DUTCH TEST**

1. 24-hour free cortisol

2. 24-hour free cortisone
3. Daily free cortisol pattern, so is cortisol produced in the proper diurnal fashion
4. Daily free cortisone pattern
5. Balance between cortisol and cortisone
6. Metabolized cortisol, which is a combination of tetrahydrocortisol and tetrahydrocortisone, and this is the best indicator of total or overall cortisol production.
7. Total DHEA production, which is DHEA sulfate plus etiocholanolone plus androsterone
8. Melatonin

### **THERE ARE SIX FREE CORTISOL PATTERNS:**

1. Normal
2. High free cortisol
  - a. Perceived stress
  - b. Inflammation
  - c. Circadian disruption
  - d. Cushing's syndrome/disease. There is virtually no diurnal drop in cortisol, which means the midnight reading will be almost the same as the waking reading. In pseudo-Cushing's syndrome, patients still have circadian rhythm, but the late morning, afternoon, evening, and midnight readings are higher. You would see a nighttime value that is three to four times above the lab range, and then you would look for high cortisol metabolites.
3. High evening/nighttime cortisol
  - a. Depression
  - b. Sleep deprivation. Patient might be a night owl and get a second wind at night.
  - c. PTSD
  - d. Cognitive impairment
  - e. Low bone density
  - f. Circadian disruption
  - g. PCOS
  - h. Type 2 diabetes
  - i. Cushing's syndrome/disease.

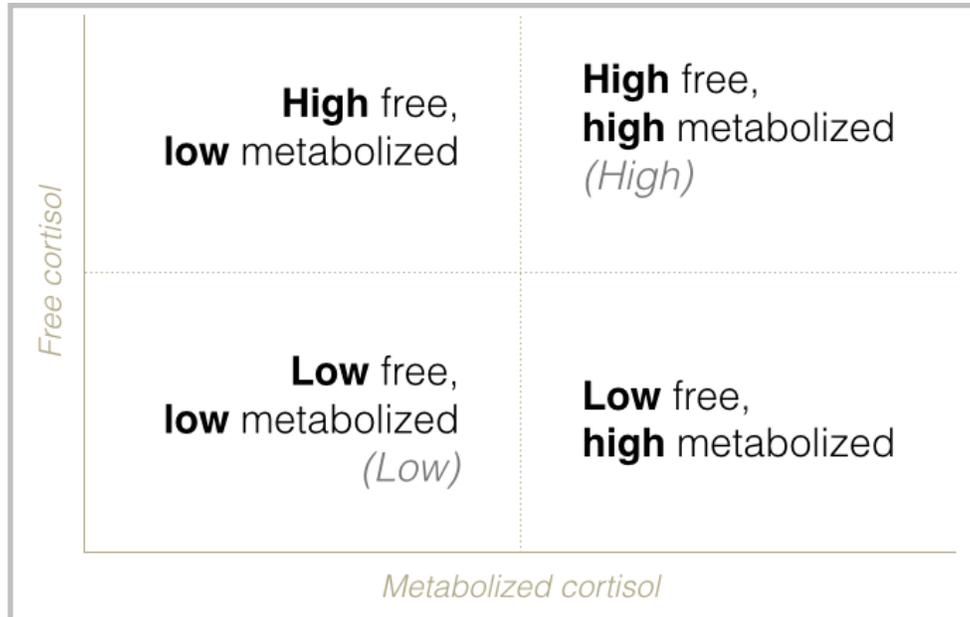
Very high waking cortisol often indicates overproduction of cortisol through the night. This would explain why a patient might be waking up throughout the night because their cortisol is high. It can have a suppressive effect on melatonin.

4. Disrupted diurnal cortisol rhythm
  - a. Sleep disturbance
  - b. Circadian disruption
  - c. Perceived stress
  - d. Fatigue
  - e. Trauma
  - f. Flipped diurnal rhythm. Patients can have disrupted rhythm with normal cortisol. Cortisol is low when it should be high in the morning and high when it should be low at night. Common in patients with chronic fatigue. They will often feel really tired in the morning. They might have that second wind at night, but they're going to have really nonrestorative sleep and significant fatigue.
5. Hypocortisolism (normal rhythm)
6. Hypocortisolism (no rhythm)

#### **CONDITIONS ASSOCIATED WITH LOW FREE CORTISOL**

- a. Metabolic syndrome
- b. Fibromyalgia
- c. Chronic fatigue syndrome
- d. Chronic pain
- e. Cardiometabolic disease
- f. Mood disorders
- g. Autoimmune disease
- h. Cancer
- i. Addison's disease. Free cortisol below 10. Remember that Addison's disease is rare. Most cases of very low or flat-line cortisol are caused by medication use, so both glucocorticoids and opioids can suppress cortisol production.
- j. Glucocorticoid/opioid use

#### **OVERALL CORTISOL PATTERNS**



1. High free cortisol with high metabolized cortisol
  - a. Most often seen in Cushing’s disease or pseudo-Cushing’s syndrome, high perceived stress, and inflammatory conditions such as PCOS, IBD, and depression.
  - b. Markers such as low vitamin D, functional anemia, and decreased mitochondrial function activate the HPA axis and cause an increase in cortisol.
2. Low free cortisol and low metabolized cortisol
  - a. Commonly seen in Addison’s, medication-induced adrenal insufficiency (such as glucocorticoid use), trauma, PTSD, and possibly chronic fatigue syndrome. For example, remember that cortisol helps resolve the inflammatory response, so when cortisol is low, the patient can’t turn off the inflammation, which can contribute to conditions like gut issues and food sensitivities. However, the gut issues likely contribute to low cortisol levels, so you can see a vicious cycle.
3. Low free cortisol and high metabolized cortisol
  - a. Main causes are obesity, insulin resistance and metabolic dysfunction, hyperthyroidism, chronic stress, glucocorticoid use, and chronic fatigue syndrome.
  - b. This has been studied extensively in the literature. In obesity, we typically see normal or low free cortisol, and then we’ll see high cortisol metabolites.
4. High free cortisol and low metabolized cortisol
  - a. Observed in hypothyroidism, licorice supplementation, inflammation, and in some cases, it may be normal and nonpathological.

## WHY IS CORTISOL ELEVATED IN OBESITY?

<p><b>Increased</b>  <b>11β-HSD1 and 5α/β-reductase</b> activity, which mean that more fat equals more cortisol in the tissues</p>	<p><b>Impaired</b>  <b>cortisol to cortisone</b> conversion</p>	<p><b>Enhanced</b>  production of <b>CRH, ACTH</b> and <b>cortisol</b></p>	<p><b>Enhanced</b>  <b>peripheral metabolism</b> of cortisol</p>
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### CORTISOL AND THYROID FUNCTION

<b>Hyperthyroidism</b>		<b>Hypothyroidism</b>	
<b>Free cortisol</b>	Low or normal	<b>Free cortisol</b>	High or normal
<b>Total metabolites</b>	High	<b>Total metabolites</b>	Low
<b>THE/a-THF ratio</b>	Increased	<b>THE/a-THF ratio</b>	Decreased

Researchers are considering using urinary cortisol metabolites or cortisol test results as a way of diagnosing subclinical hypothyroidism.

### INFLAMMATION AND CORTISOL/DHEA

<b>Free cortisol</b>	High
<b>Total metabolites</b>	Normal or low
<b>Cortisol to cortisone ratio</b>	Increased
<b>DHEA (S)</b>	Normal
<b>DHEA-Sulfate</b>	Low

DHEA sulfate is often low because inflammation inhibits sulfation.

Finally, if you see a pattern where a patient is relatively high in free cortisol in the early morning and lower the rest of the day, you might see metabolites that are lower because the DUTCH test will miss that disproportionate amount of the metabolites that come from that morning surge due to the 90-minute lag time of the urine samples. That is not necessarily a pathological finding.