



Nordic Laboratories
dutch
Direct Urine Test for Cortisol and Cortisone

PATIENT: **Sample Report**

TEST REF: **###-##-####**

TEST NUMBER: #####
 PATIENT NUMBER: #####
 GENDER: Female
 AGE: 27
 DATE OF BIRTH: dd-mm-yyyy

COLLECTED: dd/mm/yyyy
 RECEIVED: dd/mm/yyyy
 TESTED: dd/mm/yyyy

PRACTITIONER: **Nordic Laboratories**
 ADDRESS:

TEST NAME: DUTCH Adrenal

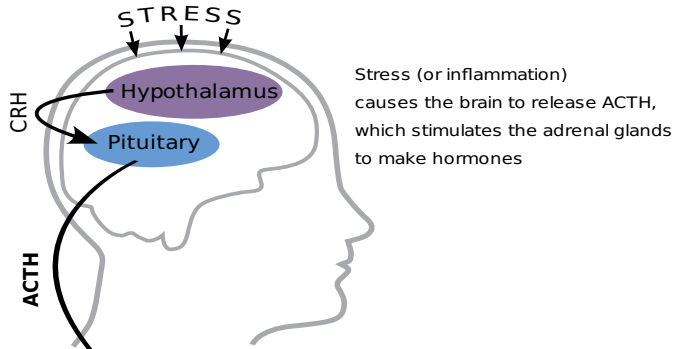
Category	Test	Result	Units	Normal Range
Creatinine (Urine)				
	Creatinine A (Waking)	Within range	0.25 mg/ml	0.2 - 2
	Creatinine B (Morning)	Within range	0.28 mg/ml	0.2 - 2
	Creatinine C (Afternoon)	Within range	0.27 mg/ml	0.2 - 2
	Creatinine D (Night)	Below range	0.13 mg/ml	0.2 - 2
Daily Free Cortisol and Cortisone (Urine)				
	Cortisol A (Waking)	Below range	3.9 ng/mg	12 - 55
	Cortisol B (Morning)	Below range	13.5 ng/mg	38 - 155
	Cortisol C (Afternoon)	Below range	6.6 ng/mg	7.3 - 30
	Cortisol D (Night)	Within range	6.1 ng/mg	0 - 14
	Cortisone A (Waking)	Below range	22.2 ng/mg	40 - 120
	Cortisone B (Morning)	Below range	71.3 ng/mg	90 - 230
	Cortisone C (Afternoon)	Low end of range	38.3 ng/mg	32 - 95
	Cortisone D (Night)	Within range	30.0 ng/mg	0 - 55
	24hr Free Cortisol	Below range	30.2 ng/mg	80 - 230
	24hr Free Cortisone	Below range	161.8 ng/mg	220 - 450
Cortisol Metabolites and DHEA-S (Urine)				
	a-Tetrahydrocortisol (a-THF)	Low end of range	113.0 ng/mg	75 - 370
	b-Tetrahydrocortisol (b-THF)	Below range	486.0 ng/mg	1050 - 2500
	b-Tetrahydrocortisone (b-THE)	Below range	1313.0 ng/mg	1550 - 3800
	Metabolized Cortisol (THF+THE)	Below range	1912.0 ng/mg	2750 - 6500
	DHEA-S	Within range	290.0 ng/mg	20 - 750

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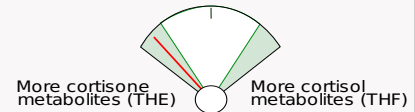
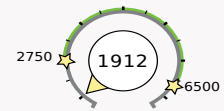
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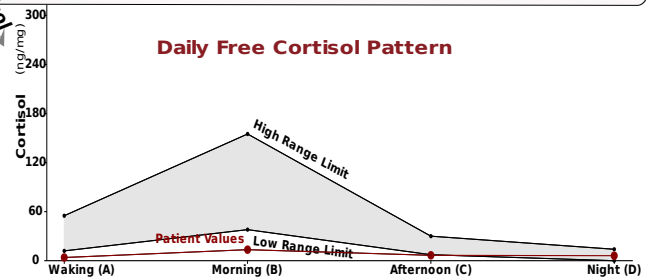
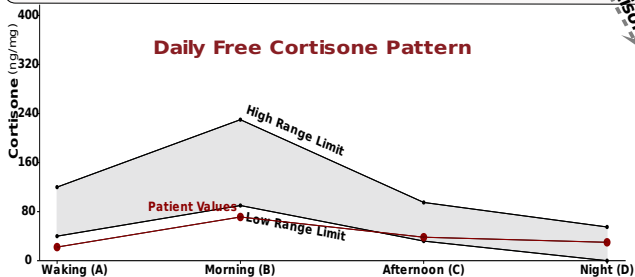


DHEA-S Ranges

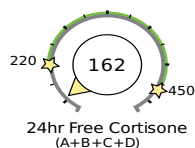
Age	Range
20-39	60-750
40-60	30-350
>60	20-150



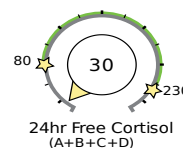
NOTE: This 11b-HSD index measures the balance of cortisol and cortisone metabolites which best reflects the overall balance of active cortisol and inactive cortisone systemically.



At least one sample has a very low creatinine (female <0.15; male <0.2, see page 4), and for these individual samples cortisol & cortisone values may be somewhat less reliable.



Cortisol and Cortisone interconvert (11b-HSD)



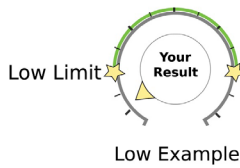
The first value reported (Waking "A") for cortisol is intended to represent the "overnight" period. When patients sleep through the night, they collect just one sample. In this case, the patient did not report waking up during the night to collect a sample, so the "Waking (A)" cortisol and cortisone values should accurately represent the entirety of the overnight period.

TEST NAME: DUTCH Adrenal

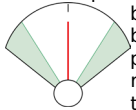
Provider Notes

How to read the DUTCH report

The graphic dutch dials in this report are intended for quick and easy evaluation of which hormones are out of range. Results below the left star are shaded yellow and are below range (left). Results between the stars and shaded green are within the reference range (middle). Results beyond the second star and shaded red are above the reference range (right). Some of these hormones also change with age, and the age-dependent ranges provided should also be considered.



In a few places on the graphical pages, you will see fan-style gauges. For sex hormones, you will see one for the balance between 5a/5b metabolism as well as methylation. For adrenal hormones, you will see one to represent the balance between cortisol and cortisolone metabolites. These indexes simply look at the ratio of hormones for a preference. An average or "normal" ratio between the two metabolites (or groups of metabolites) will give a result in the middle (as shown here). If the ratio between the metabolites measured is "low" the gauge will lean to the left and similarly to the right if the ratio is higher than normal.



Patient or Sample Comments

Throughout the provider comments you may find some comments specific to your situation or results. These comments will be found in this section or within another section as appropriate. Comments in other sections that are specific to your case will be in **bold**.

The patient reports irregular menstrual cycles.

The patient reported symptoms of excess estrogen. This can be caused by excess estrogen or progesterone deficiency. Results should be carefully reviewed. We do not report a progesterone to estrogen ratio. However, you can investigate this issue by looking at the relative level of these two hormones on their respective gauges.

The patient reports significant symptoms of both androgen deficiency and excess. Results and symptoms should be reviewed carefully.

The patient reported significant fatigue in both the AM and PM.

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 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. Remember that with urine results, the "waking" sample reflects the night's total for free cortisol. The sample collected two hours after waking captures the cortisol awakening response, which is typically the time with the most cortisol secretion.



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• The sum of the free cortisol as an expression of the overall tissue cortisol exposure:

This total of four free cortisol measurements is the best way to assess the total of free cortisol throughout the day, and this result correlates reasonably well to a true 24-hour urine free cortisol. Do be aware that this measurement does not take into account transitory shifts in cortisol in the late morning or early afternoon.

• The total level of cortisol metabolites:

We call this calculation "Metabolized Cortisol" which is the sum of a-THF, b-THF and b-THE (the most abundant cortisol metabolites). While free cortisol is the best assessment for tissue levels of cortisol, it only represents 1-3% of the total produced. The majority of cortisol results in a urine metabolite and the total of these metabolites best represents the total glandular output of cortisol for the day. When overall production is much higher than free cortisol levels, cortisol clearance may be increased (as seen in hyperthyroidism, obesity, etc.) The most common reason for sluggish cortisol clearance (assumed when free cortisol levels are much higher than metabolized cortisol) is low thyroid.

Free cortisol levels are low. Low overall HPA-Axis activity is confirmed by low levels of metabolized cortisol.

• A potential preference for cortisol or cortisone (the inactive form):

Looking at the comparison between the total for free cortisol and free cortisone is NOT the best indication of a person's preference for cortisol or cortisone. The kidney converts cortisol to cortisone in the local tissue. This localized conversion can be seen by comparing cortisol (free) and cortisone levels. To see the patient's preference systemically, it is best to look at which *metabolite* predominates (THF or THE). This preference can be seen in the fan style gauge. This is known as the 11b-HSD index. The enzyme 11b-HSD II converts cortisol to cortisone in the kidneys, saliva gland and colon. 11b-HSD I is more active in the liver, fat cells and the periphery and is responsible for reactivating cortisone to cortisol. Both are then metabolized by 5a-reductase to become tetrahydrocortisol (THF) and tetrahydrocortisone (THE) respectively.

Urine Hormone Testing - General Information

What is actually measured in urine? In blood, most hormones are bound to binding proteins. A small fraction of the total hormone levels are "free" and unbound such that they are active hormones. These free hormones are not found readily in urine except for cortisol and cortisone (because they are much more water soluble than, for example, testosterone). As such, free cortisol and cortisone can be measured in urine and it is this measurement that nearly all urinary cortisol research is based upon. In the DUTCH Adrenal Profile the diurnal patterns of free cortisol and cortisone are measured by LC-MS/MS.

All other hormones measured (cortisol metabolites, DHEA, and all sex hormones) are excreted in urine predominately after the addition of a glucuronide or sulfate group (to increase water solubility for excretion). As an example, Tajic (Natural Sciences, 1968 publication) found that of the testosterone found in urine, 57-80% was testosterone-glucuronide, 14-42% was testosterone-sulfate, and negligible amounts (<1% for most) was free testosterone. The most likely source of free sex hormones in urine is from contamination from hormonal supplements. To eliminate this potential, we remove free hormones from conjugates (our testing can be used even if vaginal hormones have been given). The glucuronides and sulfates are then broken off of the parent hormones, and the measurement is made. These measurements reflect the bioavailable amount of hormone in most cases as it is only the free, nonprotein-bound fraction in blood/tissue that is available for phase II metabolism (glucuronidation and sulfation) and subsequent urine excretion.

Disclaimer: the filter paper used for sample collection is designed for blood collection, so it is technically considered "research only" for urine collection. Its proper use for urine collection has been thoroughly validated.

Nordic Laboratories Aps

Nygade 6, 3.sal • 1164 Copenhagen K • Denmark
Tel: +45 33 75 10 00

UK Office:

11 Old Factory Buildings • Stonegate • E. Sussex TN5 7DU • UK
Tel: +44 (0)1580 201 687

Page 4 of 5

www.nordiclabs.com
info@nordiclabs.com



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Reference Range Determination (last updated 11.15.2017)

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 06.06.2018)									
	Low%	High%	Low	High		Low%	High%	Low	High
b-Pregnanediol	20%	90%	600	2000	Cortisol A (waking)	20%	90%	12	55
a-Pregnanediol	20%	90%	200	740	Cortisol B (morning)	20%	90%	38	155
Estrone (E1)	20%	80%	12	26	Cortisol C (~5pm)	20%	90%	7.3	30
Estradiol (E2)	20%	80%	1.8	4.5	Cortisol D (bed)	0	90%	0	14
Estriol (E3)	20%	80%	5	18	Cortisone A (waking)	20%	90%	40	120
2-OH-E1	20%	80%	5.1	13.1	Cortisone B (morning)	20%	90%	90	230
4-OH-E1	0	80%	0	1.8	Cortisone C (~5pm)	20%	90%	32	95
16-OH-E1	20%	80%	0.7	2.6	Cortisone D (bed)	0	90%	0	55
2-Methoxy-E1	20%	80%	2.5	6.5	Melatonin (6-OHMS)	20%	90%	10	85
2-OH-E2	0	80%	0	1.2	8-OHdG	0	90%	0	5.2
4-OH-E2	20%	80%	0.15	0.5	Methylmalonate	0	90%	0	2.2
2-Methoxy-E2	20%	80%	0.3	0.7	Xanthurenate	0	90%	0	1.4
DHEA-S	20%	90%	20	750	Pyroglutamate	10%	90%	32	60
Androsterone	20%	80%	200	1650	Homovanillate	10%	95%	4	13
Etiocholanolone	20%	80%	200	1000	Vanilmandelate	10%	95%	2.4	6.4
Testosterone	20%	80%	2.3	14	5-Hydroxyindoleacetate	10%	95%	2.5	7.5
5a-DHT	20%	80%	0	6.6	Calculated Values				
5a-Androstanediol	20%	80%	12	30	Total DHEA Production	20%	80%	500	3000
5b-Androstanediol	20%	80%	20	75	Total Estrogens	20%	80%	35	70
Epi-Testosterone	20%	80%	2.3	14	Metabolized Cortisol	20%	90%	2750	6500
a-THF	20%	90%	75	370	24hr Free Cortisol	20%	90%	80	230
b-THF	20%	90%	1050	2500	24hr Free Cortisone	20%	90%	220	450
b-THE	20%	90%	1550	3800					

% = 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."

Provider Notes:
