



**Accession # 00908316**  
 Female Sample Report  
 123 A Street  
 Sometown, CA 90266



**Adrenal**

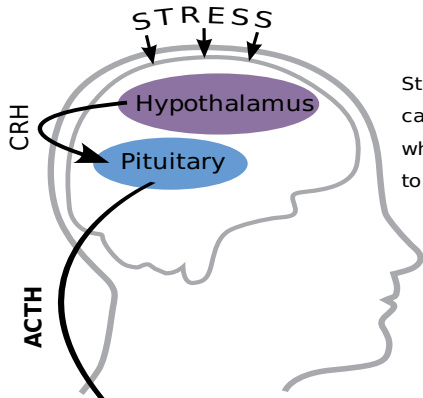
**Last Menstrual Period:**

**Ordering Provider:**  
 Precision Analytical

**DOB:** 1990-09-01  
**Age:** 33  
**Sex:** Female

**Collection Times:**  
 2024-04-25 02:00AM  
 2024-04-25 08:00AM  
 2024-04-25 10:00AM  
 2024-04-25 05:00PM  
 2024-04-25 10:00PM

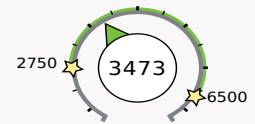
Category	Test	Result	Units	Normal Range
<b>Creatinine (Urine)</b>				
	Creatinine A (Waking)	Within range	1.0 mg/ml	0.2 - 2
	Creatinine B (Morning)	Within range	0.8 mg/ml	0.2 - 2
	Creatinine C (Afternoon)	Within range	0.8 mg/ml	0.2 - 2
	Creatinine D (Night)	Within range	0.6 mg/ml	0.2 - 2
<b>Daily Free Cortisol and Cortisone (Urine)</b>				
	Cortisol A (Waking)	Low end of range	14.6 ng/mg	10 - 50
	Cortisol B (Morning)	Within range	77.2 ng/mg	30 - 130
	Cortisol C (Afternoon)	High end of range	25.7 ng/mg	7 - 30
	Cortisol D (Night)	Within range	3.4 ng/mg	0 - 14
	Cortisone A (Waking)	Within range	66.2 ng/mg	40 - 120
	Cortisone B (Morning)	Within range	199.0 ng/mg	90 - 230
	Cortisone C (Afternoon)	Within range	87.2 ng/mg	32 - 110
	Cortisone D (Night)	Within range	19.7 ng/mg	0 - 55
	24hr Free Cortisol	Within range	120.9 ng/mg	65 - 200
	24hr Free Cortisone	Within range	372.1 ng/mg	220 - 450
<b>Cortisol Metabolites and DHEA-S (Urine)</b>				
	a-Tetrahydrocortisol (a-THF)	Low end of range	130.3 ng/mg	75 - 370
	b-Tetrahydrocortisol (b-THF)	Within range	1349.8 ng/mg	1050 - 2500
	b-Tetrahydrocortisone (b-THE)	Low end of range	1993.2 ng/mg	1550 - 3800
	Metabolized Cortisol (THF+THE)	Low end of range	3473.4 ng/mg	2750 - 6500
	DHEA-S	Low end of range	38.8 ng/mg	20 - 750



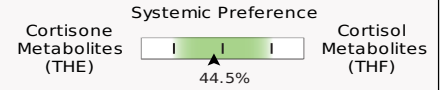
Stress (or inflammation) causes the brain to release ACTH, which stimulates the adrenal glands to make hormones

**DHEA-S Ranges**

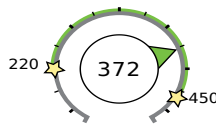
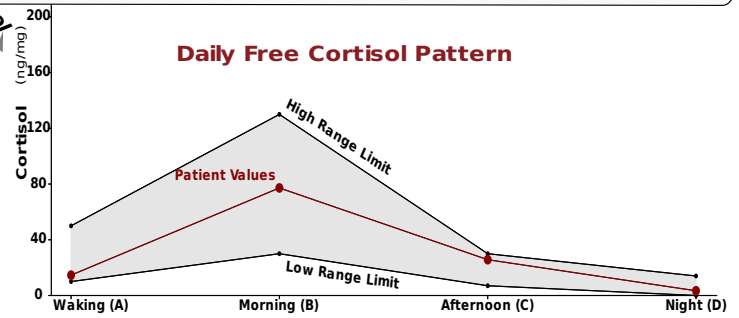
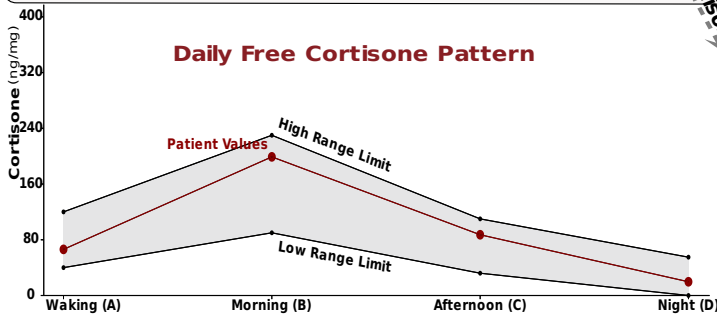
Age	Range
20-39	60-750
40-60	30-350
>60	20-150



Metabolized Cortisol (THF+THE) (Total Cortisol Production)

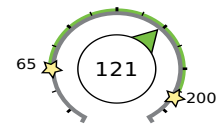


NOTE: This 11b-HSD index measures the balance of cortisol and cortisone metabolites which best reflects the overall balance of active cortisol and inactive cortisone systemically.



24hr Free Cortisone (A+B+C+D)

Cortisol and Cortisone interconvert (11b-HSD)



24hr Free Cortisol (A+B+C+D)

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 woke during the night and collected (see the top of the report for the times collected). We call this value "A1" and the value from the sample collected at waking "A2." These values are used to create a "time-weighted average" to create the "A" value. The individual values are listed here for your use:

**The middle-of-the-night "A1" sample registered a cortisol value of 3.80ng/mg.**

**The waking "A2" sample registered a cortisol value of 23.4ng/mg.**

**These two values are averaged together, taking into account the amount of time each one represents, to create the "A" value of approximately 14.6ng/mg that you will see on the report.**

# Clinical Support Overview

Thank you for choosing DUTCH for your functional endocrinology testing needs! We know you have many options to choose from when it comes to functional endocrinology evaluation, and we strive to offer the best value, the most up-to-date testing parameters and reference ranges, and the greatest clinical support to ensure the most accurate results.

Please take a moment to read through the Clinical Support Overview below. These comments are specific to the patient's lab results. They detail the most recent research pertaining to the hormone metabolites, treatment considerations, and follow-up recommendations. These comments are intended for educational purposes only. Specific treatment should be managed by a healthcare provider. To view the steroid pathway chart, click here [Steroid Pathway Chart](#)

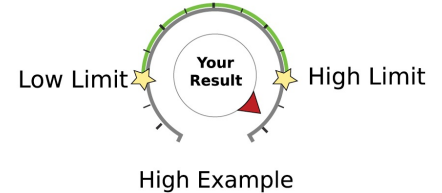
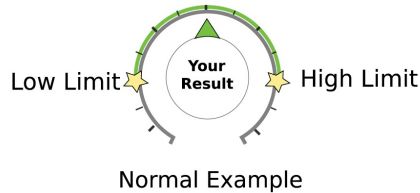
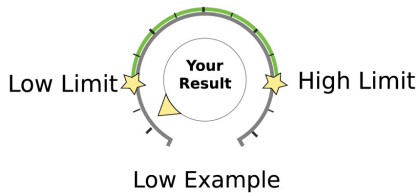
## Alert comments:

## How to read the DUTCH report

This report is not intended to treat, cure or diagnose any specific diseases.

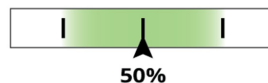
### DUTCH Dials

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### DUTCH Slider Bars

In a few places on the graphic pages, you will see slider bars. For adrenal hormones, you will see one to represent the balance between cortisol and cortisone metabolites. These bars indicate the relative ratio of the metabolites noted. The percentage stated is a population percentage, and so a result of 50%, as in this example (with the slider arrow in the middle of the bar) indicates that the ratio is higher than 50% of individuals tested, or right in the middle of the population's range. If the ratio between the metabolites is "low", the arrow will slide to the left and represent a smaller percentage and similarly to the right if the ratio is higher than normal. For more information about the new slider bars, please click to read our [DUTCH Blog](#)



### 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 following video link(s) may help those new to dutch testing to understand the results. If you only have a hardcopy of the results, the video names can be easily found in our video library at [www.DutchTest.com](http://www.DutchTest.com). Be aware that our reporting format has recently undergone some cosmetic changes, so the results on the video may look slightly different. These results and videos are NOT intended to diagnose or treat specific disease states.

This video may assist with the interpretation of the Adrenal (cortisol) results: [Cortisol tutorial video](#)

### The patient reports regular menstrual cycles.

### 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 and the hippocampus, where ACTH normally surges right after waking leading to the day's highest levels of cortisol. This signal 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, some psychosocial factors such as depression or anxiety and their 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. Free cortisol 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 to get a bigger picture.

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 assess both metabolized cortisol and free cortisol.

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

- **The daily 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.

- **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 consider transitory shifts in cortisol in the late morning or early afternoon. This number is calculated from the simple addition of the 4 points, so if a single point is very high or very low, it may skew the number up or down especially if it is the morning "B" point, as it is weighted more heavily in the reference range.

- **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 total metabolized cortisol best represents the total glandular output of cortisol for the day, closer to 80% of the total produced.

**Overall cortisol levels are appropriate as both free and metabolized cortisol levels are within range. If the diurnal pattern of the free cortisol is as expected, this implies normal HPA-Axis cortisol production.**

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

To determine total systemic preference for cortisol or cortisone, it is best to look at which *metabolite* predominates (THF or THE?). This preference can be seen in the slider bar. 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. We can see more cortisol or cortisone in different metabolic conditions. For example, a preference for cortisol indicates possible inflammation, insulin resistance or hypothyroidism. A preference for cortisone can indicate chronic stress or chronic infection (such as the later stages of a virus or common cold).

### 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.

## Reference Range Determination (last updated 5.1.2024)

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 05.1.2024)									
	Low%	High%	Low	High		Low%	High%	Low	High
b-Pregnanediol	20%	90%	600	2000	Cortisol A (waking)	20%	90%	10	50
a-Pregnanediol	20%	90%	200	740	Cortisol B (morning)	20%	90%	30	130
Estrone (E1)	20%	80%	12	26	Cortisol C (~5pm)	20%	90%	7	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	110
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	0	80%	0	0.5	Methylmalonate	0	90%	0	2.5
2-16-ratio	20%	80%	2.69	11.83	Xanthurenate	0	90%	0.12	1.2
2-4-ratio	20%	80%	5.4	12.62	Kynurenate	0	90%	0.8	4.5
2Me-2OH-ratio	20%	80%	0.39	0.67	b-Hydroxyisovalerate	0	90%	0	12.5
DHEA-S	20%	90%	20	750	Pyroglutamate	10%	90%	28	58
Androsterone	20%	80%	200	1650	Indican	0	90%	0	100
Etiocholanolone	20%	80%	200	1000	Homovanillate	10%	95%	3	11
Testosterone	20%	80%	2.3	14	Vanilmandelate	10%	95%	2.2	5.5
5a-DHT	0	80%	0	6.6	Quinolate	0	90%	0	9.6
5a-Androstanediol	20%	80%	6	30					
5b-Androstanediol	20%	80%	20	75					
Epi-Testosterone	20%	80%	2.3	14	<b>Calculated Values</b>				
a-THF	20%	90%	75	370	Total DHEA Production	20%	80%	500	3000
b-THF	20%	90%	1050	2500	Total Estrogens	20%	80%	35	70
b-THE	20%	90%	1550	3800	Metabolized Cortisol	20%	90%	2750	6500
					24hr Free Cortisol	20%	90%	65	200
					24hr Free Cortisone	20%	90%	220	450

*% = 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."*



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**Adrenal**

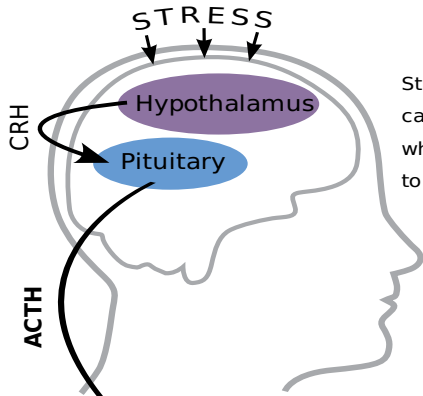
**Ordering Provider:**  
 Precision Analytical

**DOB:** 1967-08-09  
**Age:** 56  
**Sex:** Male

**Collection Times:**  
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Category	Test	Result	Units	Normal Range
<b>Creatinine (Urine)</b>				
	Creatinine A (Waking)	Within range	0.77 mg/ml	0.3 - 3
	Creatinine B (Morning)	Within range	0.6 mg/ml	0.3 - 3
	Creatinine C (Afternoon)	Within range	0.55 mg/ml	0.3 - 3
	Creatinine D (Night)	Below range	0.29 mg/ml	0.3 - 3
<b>Daily Free Cortisol and Cortisone (Urine)</b>				
	Cortisol A (Waking)	Within range	35.0 ng/mg	13 - 80
	Cortisol B (Morning)	Within range	76.6 ng/mg	35 - 180
	Cortisol C (Afternoon)	Within range	30.2 ng/mg	10 - 45
	Cortisol D (Night)	Within range	7.8 ng/mg	0 - 20
	Cortisone A (Waking)	Within range	83.5 ng/mg	40 - 160
	Cortisone B (Morning)	Within range	138.9 ng/mg	80 - 240
	Cortisone C (Afternoon)	Within range	68.5 ng/mg	40 - 130
	Cortisone D (Night)	Within range	12.7 ng/mg	0 - 70
	24hr Free Cortisol	Within range	149.6 ng/mg	75 - 300
	24hr Free Cortisone	Within range	303.6 ng/mg	220 - 550
<b>Cortisol Metabolites and DHEA-S (Urine)</b>				
	a-Tetrahydrocortisol (a-THF)	Within range	466.2 ng/mg	175 - 700
	b-Tetrahydrocortisol (b-THF)	Below range	1280.0 ng/mg	1750 - 4000
	b-Tetrahydrocortisone (b-THE)	Below range	1721.8 ng/mg	2350 - 5800
	Metabolized Cortisol (THF+THE)	Below range	3468.0 ng/mg	4550 - 10000
	DHEA-S	Low end of range	41.5 ng/mg	30 - 1500

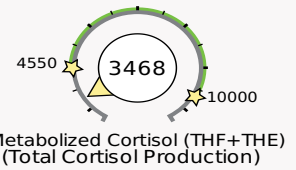




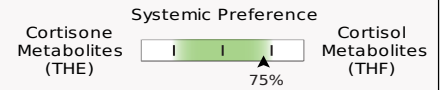
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**DHEA-S Ranges**

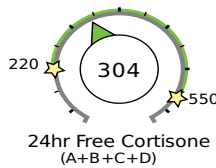
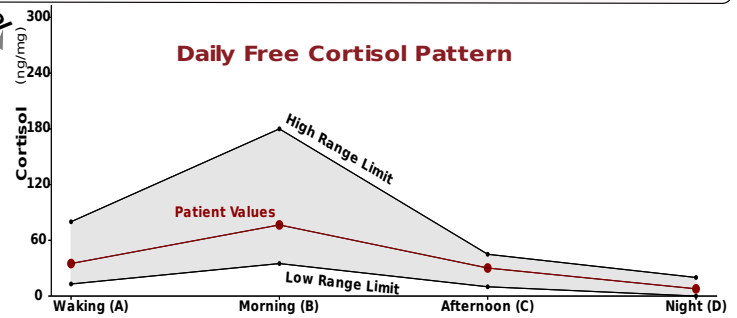
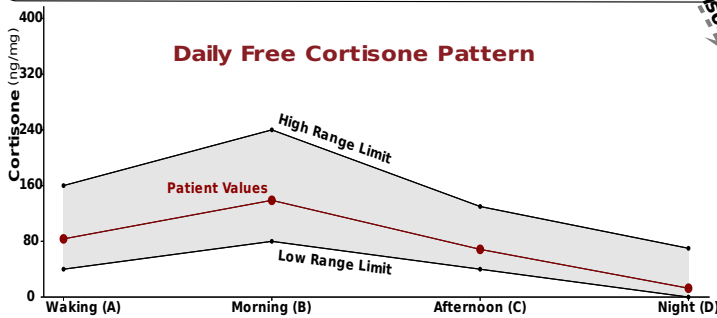
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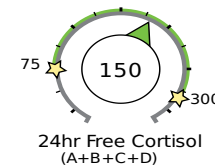
Metabolized Cortisol (THF+THE) (Total Cortisol Production)



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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 woke during the night and collected (see the top of the report for the times collected). We call this value "A1" and the value from the sample collected at waking "A2." These values are used to create a "time-weighted average" to create the "A" value. The individual values are listed here for your use:

**The middle-of-the-night "A1" sample registered a cortisol value of 13.3ng/mg.**

**The waking "A2" sample registered a cortisol value of 69.2ng/mg.**

**These two values are averaged together, taking into account the amount of time each one represents, to create the "A" value of approximately 35.0ng/mg that you will see on the report.**

**Typically, the "B" sample in the early morning is collected about 120 minutes after the waking sample. In this case the sample appears to have been collected at a time significantly outside this window or on a different day. Please interpret with care.**

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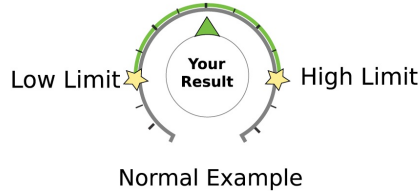
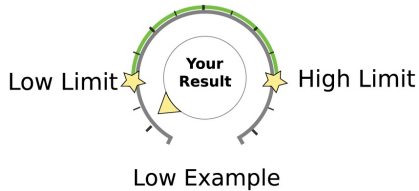
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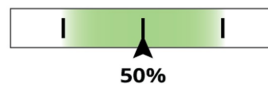
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### Patient or Sample Comments

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 following video link(s) may help those new to dutch testing to understand the results. If you only have a hardcopy of the results, the video names can be easily found in our video library at [www.DutchTest.com](http://www.DutchTest.com). Be aware that our reporting format has recently undergone some cosmetic changes, so the results on the video may look slightly different. These results and videos are NOT intended to diagnose or treat specific disease states.

This video may assist with the interpretation of the Adrenal (cortisol) results: [Cortisol tutorial video](#)

### 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 and the hippocampus, where ACTH normally surges right after waking leading to the day's highest levels of cortisol. This signal 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, some psychosocial factors such as depression or anxiety and their 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. Free cortisol 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 to get a bigger picture.

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 assess both metabolized cortisol and free cortisol.

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

- **The daily 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.

- **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 consider transitory shifts in cortisol in the late morning or early afternoon. This number is calculated from the simple addition of the 4 points, so if a single point is very high or very low, it may skew the number up or down especially if it is the morning "B" point, as it is weighted more heavily in the reference range.

- **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 total metabolized cortisol best represents the total glandular output of cortisol for the day, closer to 80% of the total produced.

**Overall free cortisol levels are within range, but metabolized cortisol (the best marker for overall cortisol production) is low. This implies that overall HPA-Axis is low. Cortisol clearance may be a bit sluggish, which keeps free cortisol levels within range in spite of low overall production. Hypothyroidism and other conditions may lead to slow cortisol metabolism. If treating the patient for potential thyroid issues be sure to take into account the interplay between the thyroid and adrenals.**

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

To determine total systemic preference for cortisol or cortisone, it is best to look at which *metabolite* predominates (THF or THE?). This preference can be seen in the slider bar. 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. We can see more cortisol or cortisone in different metabolic conditions. For example, a preference for cortisol indicates possible inflammation, insulin resistance or hypothyroidism. A preference for cortisone can indicate chronic stress or chronic infection (such as the later stages of a virus or common cold).

### 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. 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.

### Reference Range Determination (last updated 5.1.2024)

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:

Male Reference Ranges (Updated 05.1.2024)									
	Low%	High%	Low	High		Low%	High%	Low	High
b-Pregnanediol	10%	90%	75	400	Cortisol A (waking)	20%	90%	13	80
a-Pregnanediol	10%	90%	20	130	Cortisol B (morning)	20%	90%	35	180
Estrone (E1)	10%	90%	4	16	Cortisol C (~5pm)	20%	90%	10	45
Estradiol (E2)	10%	90%	0.5	2.2	Cortisol D (bed)	0	90%	0	20
Estriol (E3)	10%	90%	2	8	Cortisone A (waking)	20%	90%	40	160
2-OH-E1	0	90%	0	5.9	Cortisone B (morning)	20%	90%	80	240
4-OH-E1	0	90%	0	0.8	Cortisone C (~5pm)	20%	90%	40	130
16-OH-E1	0	90%	0	1.2	Cortisone D (bed)	0	90%	0	70
2-Methoxy-E1	0	90%	0	2.8	Melatonin (6-OHMS)	20%	90%	10	85
2-OH-E2	0	90%	0	0.6	8-OHdG	0	90%	0	8.8
4-OH-E2	0	90%	0	0.3	Methylmalonate	0	90%	0	3.5
2-16-ratio	20%	80%	2.85	9.88	Xanthurenate	0	90%	0.2	1.9
2-4-ratio	20%	80%	6.44	12.6	Kynurenate	0	90%	1	6.6
2Me-2OH-ratio	20%	80%	0.4	0.7	b-Hydroxyisovalerate	0	90%	0	18
DHEA-S	20%	90%	30	1500	Pyroglutamate	10%	90%	38	83
Androsterone	20%	80%	500	3000	Indican	0	90%	0	131
Etiocholanolone	20%	80%	400	1500	Homovanillate	10%	95%	4	16
Testosterone	20%	90%	25	115	Vanilmandelate	10%	95%	2.5	7.5
5a-DHT	20%	90%	5	25	Quinolinatate	0	90%	0	12.5
5a-Androstenediol	20%	90%	30	250					
5b-Androstenediol	20%	90%	40	250	<b>Calculated Values</b>				
Epi-Testosterone	20%	90%	25	115	Total DHEA Production	20%	80%	1000	5500
a-THF	20%	90%	175	700	Total Estrogens	10%	90%	10	34
b-THF	20%	90%	1750	4000	Metabolized Cortisol	20%	90%	4550	10000
b-THE	20%	90%	2350	5800	24hr Free Cortisol	20%	90%	75	300
					24hr Free Cortisone	20%	90%	220	550
% = 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."									