DUTCH Adrenal
Female Report

Accession # 00216507
Female Sample Report
123 A Street
Sometown, CA 90266

Adrenal

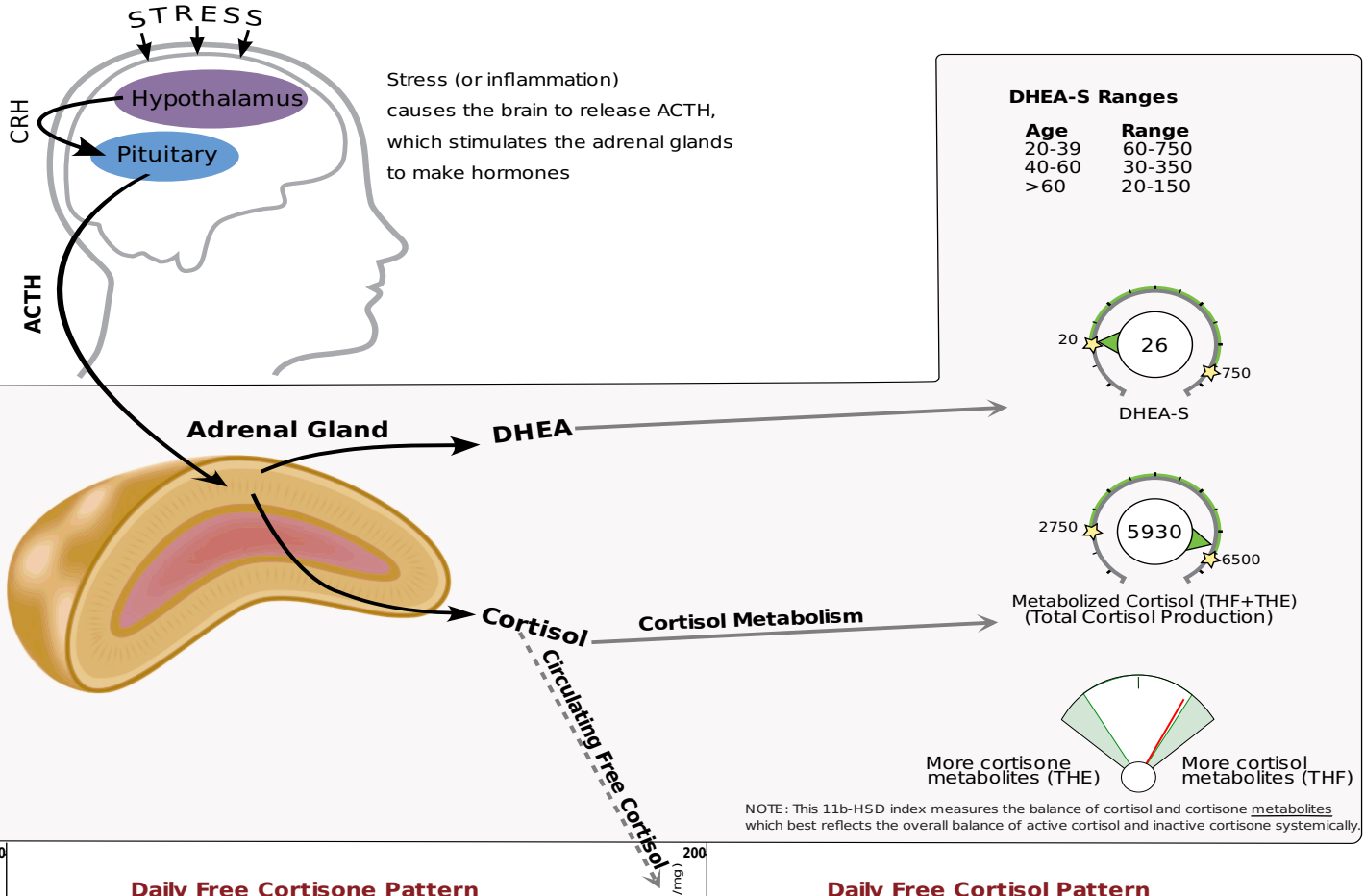
Ordering Physician:
Precision Analytical

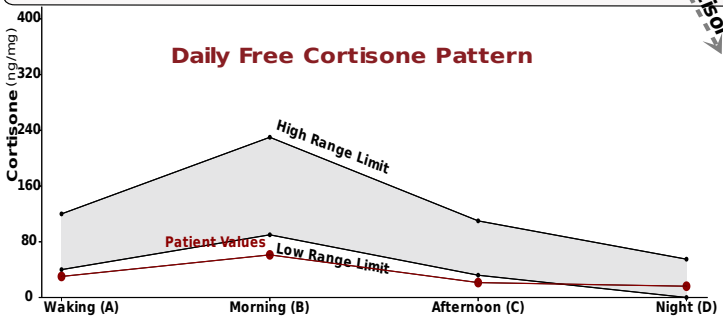
DOB: 1976-01-01
Age: 39
Gender: Female

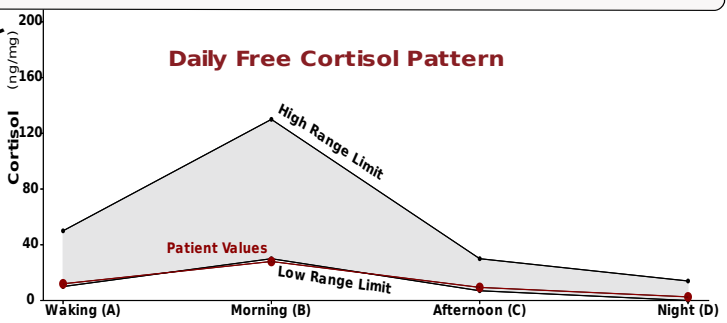
Last Menstrual Period:
2015-11-09

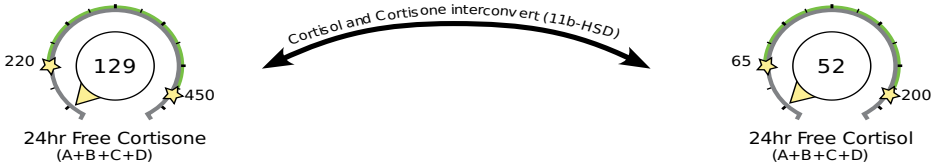
Collection Times:
2015-11-10 04:00AM
2015-11-10 06:00AM
2015-11-10 03:00PM
2015-11-10 08:00PM

Category	Test		Result	Units	Normal Range
Creatinine (Urine)					
	Creatinine A (Waking)	Within range	0.4	mg/ml	0.2 - 2
	Creatinine B (Morning)	Within range	0.51	mg/ml	0.2 - 2
	Creatinine C (Afternoon)	Within range	0.92	mg/ml	0.2 - 2
	Creatinine D (Night)	Within range	1.01	mg/ml	0.2 - 2
Daily Free Cortisol and Cortisone (Urine)					
	Cortisol A (Waking)	Low end of range	12.0	ng/mg	10 - 50
	Cortisol B (Morning)	Below range	28.0	ng/mg	30 - 130
	Cortisol C (Afternoon)	Low end of range	9.4	ng/mg	7 - 30
	Cortisol D (Night)	Low end of range	2.6	ng/mg	0 - 14
	Cortisone A (Waking)	Below range	30.2	ng/mg	40 - 120
	Cortisone B (Morning)	Below range	61.2	ng/mg	90 - 230
	Cortisone C (Afternoon)	Below range	21.4	ng/mg	32 - 110
	Cortisone D (Night)	Within range	16.2	ng/mg	0 - 55
	24hr Free Cortisol	Below range	52.0	ng/mg	65 - 200
	24hr Free Cortisone	Below range	129.0	ng/mg	220 - 450
Cortisol Metabolites and DHEA-S (Urine)					
	a-Tetrahydrocortisol (a-THF)	Above range	400.0	ng/mg	75 - 370
	b-Tetrahydrocortisol (b-THF)	Above range	2500.0	ng/mg	1050 - 2500
	b-Tetrahydrocortisone (b-THE)	Within range	3030.0	ng/mg	1550 - 3800
	Metabolized Cortisol (THF+THE)	High end of range	5930.0	ng/mg	2750 - 6500
	DHEA-S	Low end of range	26.0	ng/mg	20 - 750









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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.

As an ordering provider, we encourage you to schedule a complimentary clinical consult with one of our expert DUTCH clinicians. Please schedule via our online scheduler, email clinicalsupport@dutchtest.com or call at 503.687.2050 to schedule a 15-minute or 30-minute consultation.

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Low Example

Normal Example

High Example

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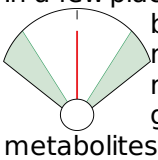

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The following video link(s) may help those new to dutch testing to understand the results. If you only have a hardcopy of the results, the video names can be easily found in our video library at www.DutchTest.com. Be aware that our reporting format 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.

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 cortisol is needed in the body, the hypothalamus releases cortisol releasing hormone (CRH) and the pituitary responds by releasing adrenocorticotropic 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 (CAR) 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. 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:**

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.

Free cortisol levels are low. Overall HPA-Axis activity may be somewhat higher than implied by free cortisol as levels of metabolized cortisol are within range. While cortisol production may be lower than needed to meet the body's demands, increased metabolism of cortisol is contributing to the lower levels of free cortisol. Increased clearance of cortisol may be caused by long-term stress, obesity, hyperthyroidism, and other conditions.

- **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. Cortisol and cortisone 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.

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 08.21.2019)

	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	20%	80%	0	0.5	Methylmalonate	0	90%	0	2.2
2-Methoxy-E2	20%	80%	0	0.7	Xanthurenate	0	90%	0	1.4
DHEA-S	20%	90%	20	750	Kynurenate	0	90%	0	7.3
Androsterone	20%	80%	200	1650	Pyroglutamate	10%	90%	32	60
Etiocholanolone	20%	80%	200	1000	Homovanillate	10%	95%	4	13
Testosterone	20%	80%	2.3	14	Vanilmandelate	10%	95%	2.4	6.4
5a-DHT	20%	80%	0	6.6					
5a-Androstanediol	20%	80%	12	30	**Calculated Values**				
5b-Androstanediol	20%	80%	20	75	Total DHEA Production	20%	80%	500	3000
Epi-Testosterone	20%	80%	2.3	14	Total Estrogens	20%	80%	35	70
a-THF	20%	90%	75	370	Metabolized Cortisol	20%	90%	2750	6500
b-THF	20%	90%	1050	2500	24hr Free Cortisol	20%	90%	65	200
b-THE	20%	90%	1550	3800	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."

Provider Notes:

DUTCH Adrenal
Male Report

Accession # 00268795
Male Sample Report
123 A Street
Sometown, CA 90266

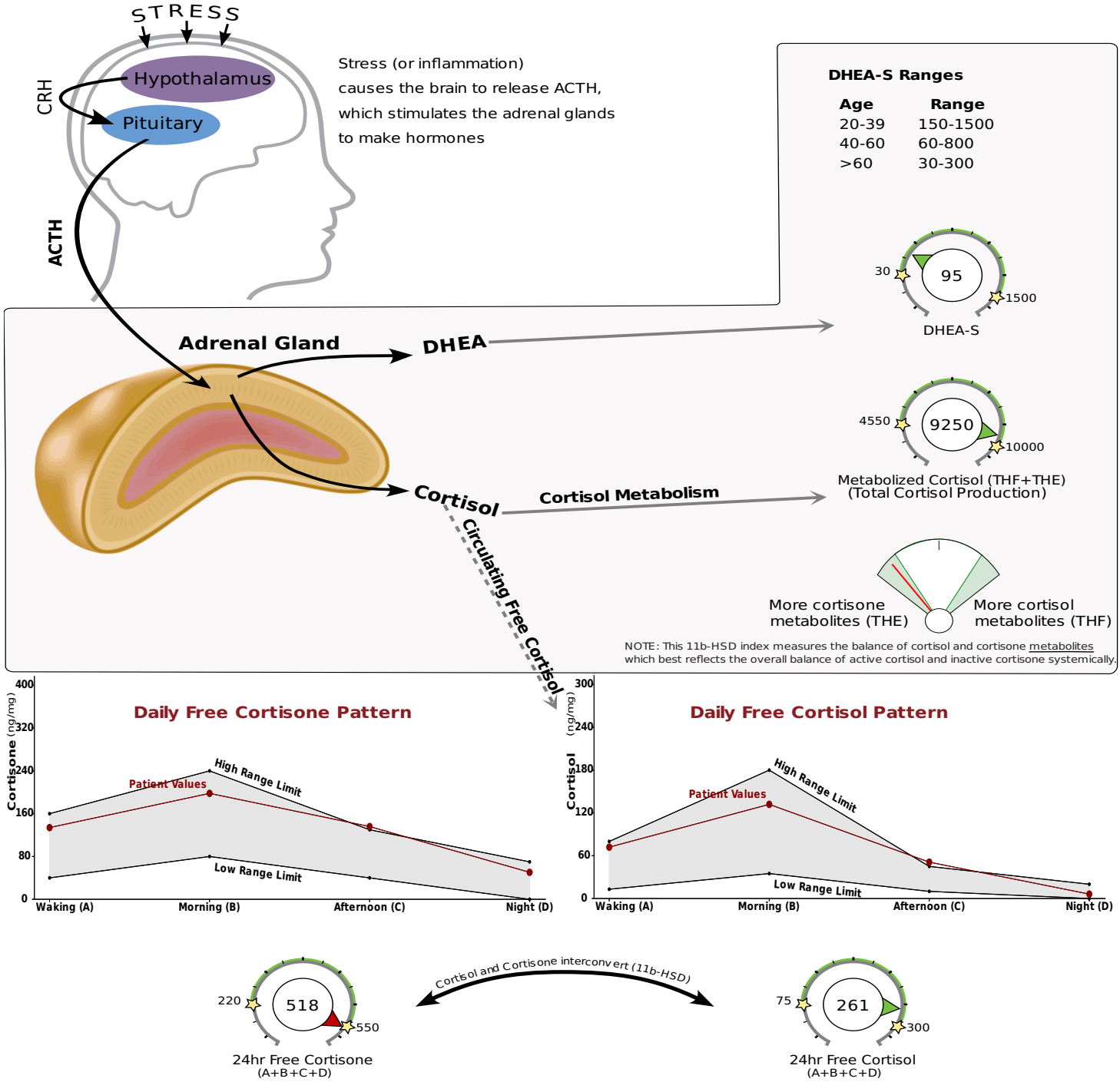
Adrenal

Ordering Physician:
Precision Analytical

DOB: 1967-08-09
Age: 50
Gender: Male

Collection Times:
2017-08-09 06:01AM
2017-08-09 08:01AM
2017-08-09 05:01PM
2017-08-09 10:01PM

Category	Test		Result	Units	Normal Range
Creatinine (Urine)					
	Creatinine A (Waking)	Within range	0.45	mg/ml	0.3 - 3
	Creatinine B (Morning)	Within range	0.41	mg/ml	0.3 - 3
	Creatinine C (Afternoon)	Within range	0.9	mg/ml	0.3 - 3
	Creatinine D (Night)	Within range	0.88	mg/ml	0.3 - 3
Daily Free Cortisol and Cortisone (Urine)					
	Cortisol A (Waking)	High end of range	72.0	ng/mg	13 - 80
	Cortisol B (Morning)	Within range	132.0	ng/mg	35 - 180
	Cortisol C (Afternoon)	Above range	51.0	ng/mg	10 - 45
	Cortisol D (Night)	Within range	6.2	ng/mg	0 - 20
	Cortisone A (Waking)	Within range	134.0	ng/mg	40 - 160
	Cortisone B (Morning)	Within range	198.0	ng/mg	80 - 240
	Cortisone C (Afternoon)	Above range	136.0	ng/mg	40 - 130
	Cortisone D (Night)	Within range	50.4	ng/mg	0 - 70
	24hr Free Cortisol	High end of range	261.2	ng/mg	75 - 300
	24hr Free Cortisone	High end of range	518.4	ng/mg	220 - 550
Cortisol Metabolites and DHEA-S (Urine)					
	a-Tetrahydrocortisol (a-THF)	Within range	450.0	ng/mg	175 - 700
	b-Tetrahydrocortisol (b-THF)	Within range	2800.0	ng/mg	1750 - 4000
	b-Tetrahydrocortisone (b-THE)	Above range	6000.0	ng/mg	2350 - 5800
	Metabolized Cortisol (THF+THE)	High end of range	9250.0	ng/mg	4550 - 10000
	DHEA-S	Low end of range	95.0	ng/mg	30 - 1500



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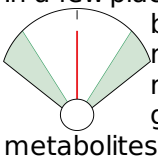

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Free cortisol provides negative feedback to CRH & ACTH. When free cortisol is too low, ACTH will surge. ACTH will also surge when a physical or psychological stressor occurs.

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.

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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:**

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While free and metabolized cortisol levels are within range, both are on the higher side of normal. This patient may have appropriate HPA-Axis function, but if they exhibit signs of excess cortisol, you may want to take efforts to calm the HPA-Axis and support the adrenals.

- **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. Cortisol and cortisone are then metabolized by 5a-reductase to become tetrahydrocortisol (THF) and tetrahydrocortisone (THE) respectively.

The patient's THF/THE ratio implies a very strong preference for the deactivation of cortisol to cortisone. In spite of this, the patient does not present with low cortisol, so the increased enzyme 11b-HSD II activity may be in response to chronically high cortisol levels. The adrenal glands may eventually have trouble keeping up with demand if adrenal support is considered, the inclusion of licorice root may be wise to avoid as it may raise the already elevated cortisol levels even more.

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

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:

Male Reference Ranges (Updated 08.21.2019)

	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)	20%	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
2-Methoxy-E2	0	90%	0	0.8	Xanthurenate	0	90%	0	2.1
DHEA-S	20%	90%	30	1500	Kynurenate	0	90%	0	9.3
Androsterone	20%	80%	500	3000	Pyroglutamate	10%	90%	43	85
Etiocholanolone	20%	80%	400	1500	Homovanillate	10%	95%	4.8	19
Testosterone	20%	90%	25	115	Vanilmandelate	10%	95%	2.8	8
5a-DHT	20%	90%	5	25					
5a-Androstanediol	20%	90%	30	250	**Calculated Values**				
5b-Androstanediol	20%	90%	40	250	Total DHEA Production	20%	80%	1000	5500
Epi-Testosterone	20%	90%	25	115	Total Estrogens	10%	90%	10	34
a-THF	20%	90%	175	700	Metabolized Cortisol	20%	90%	4550	10000
b-THF	20%	90%	1750	4000	24hr Free Cortisol	20%	90%	75	300
b-THE	20%	90%	2350	5800	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."

Provider Notes:

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