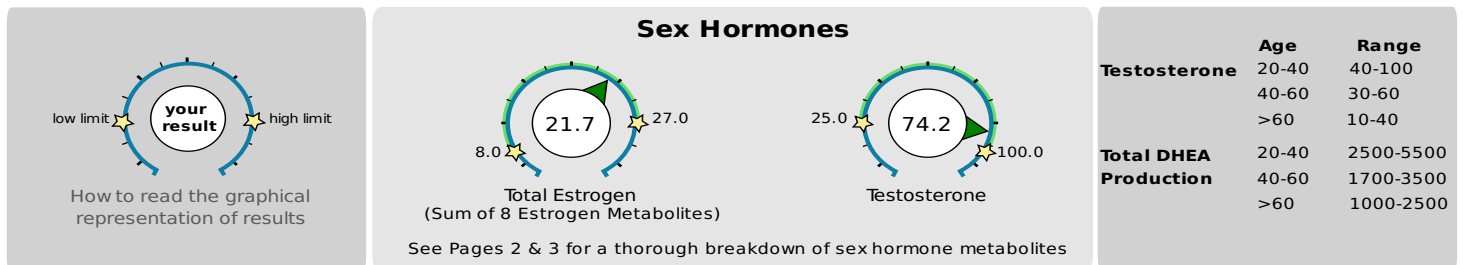


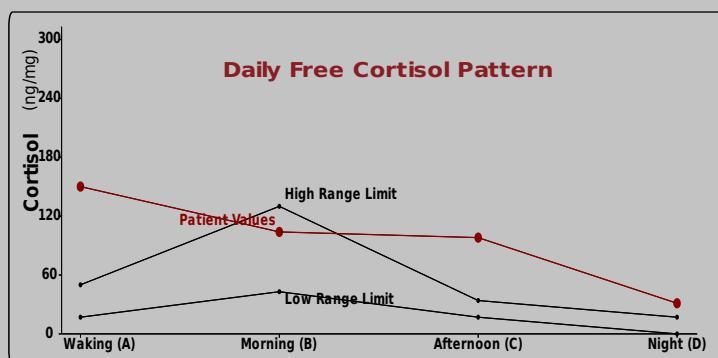
Collection Times:
2016-03-07 06:30PM
2016-03-07 11:30PM
2016-03-08 02:30AM
2016-03-08 10:30AM
2016-03-08 12:50PM

Hormone Testing Summary

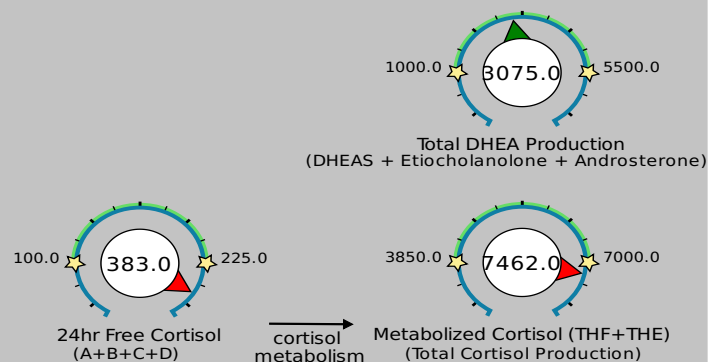
All units are given in ng/mg creatinine



Adrenal Hormones See pages 4 and 5 for a more complete breakdown of adrenal hormones



Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production.



Patient Reported Hormone Therapies: ROA 1=oral, 2=sublingual, 3=transdermal cream, 4=transdermal gel, 5=vaginal/labial, 6=rectal mucosa, 7=patch, 8=pellet, 9=injection, 10=other

| Hormone | Brand | ROA (1-10) | Dose (mg) | Date Last Used | Times per Day | Length of use |
|---|-------|------------|-----------|----------------|---------------|---------------|
| The patient did not report any relevant hormone therapies | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |

TO THE LEFT YOU CAN SEE A SCREENSHOT OF THE THERAPY SECTION OF THE PATIENT REQUISITION.

There is a series of videos in our video library at dutchtest.com that you may find useful in understanding the report. The following videos (which can also be found on the website under the listed names) may be particularly helpful in aiding your understanding:

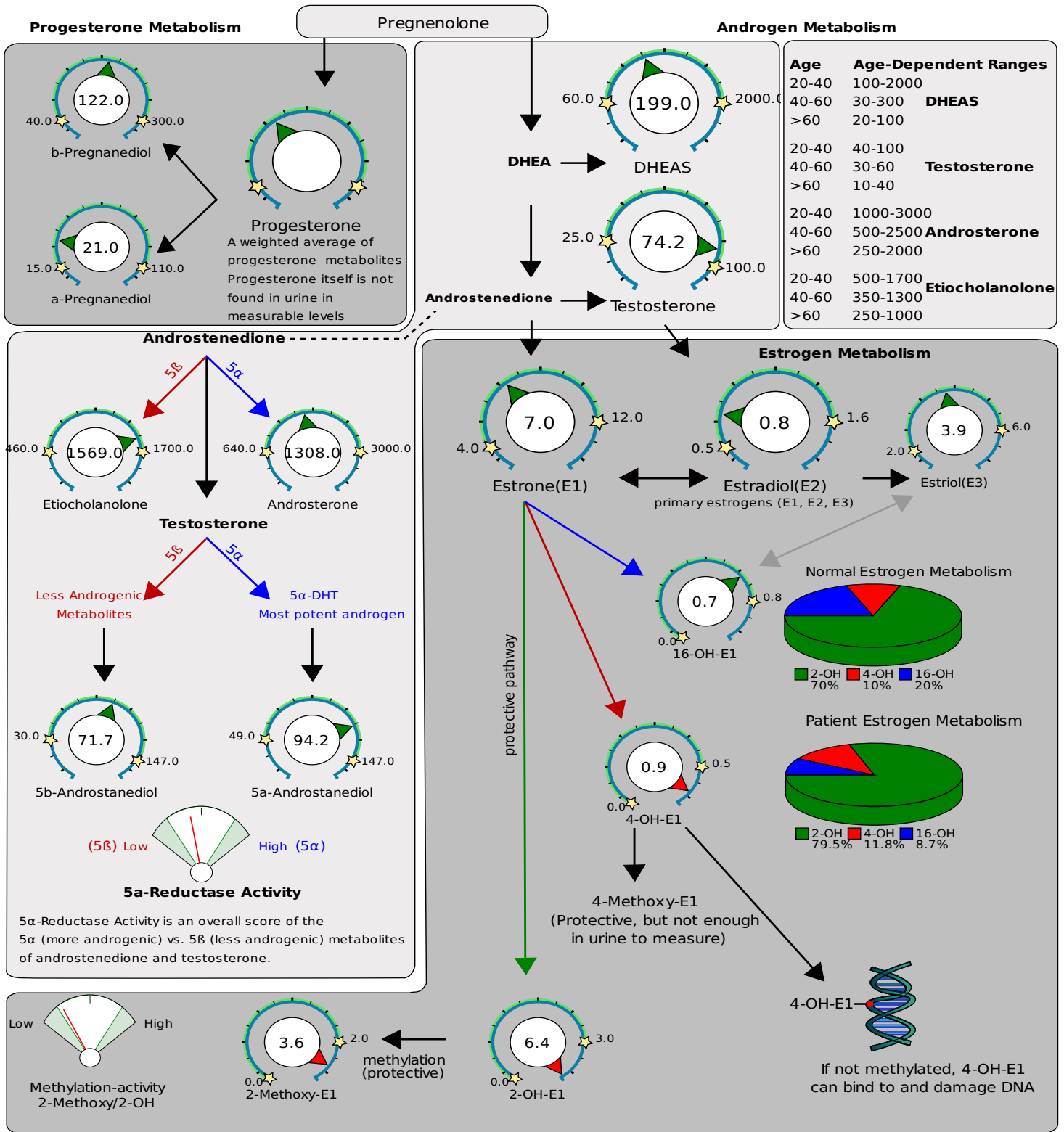
[Analytical Report Overview](#) (quick overview)
[Estrogen tutorial](#) ; [Androgen tutorial](#)
[Cortisol tutorial](#)

Collection Times:

2016-03-07 06:30PM
2016-03-07 11:30PM
2016-03-08 02:30AM
2016-03-08 10:30AM
2016-03-08 12:50PM

| Category | Test | Result | Units | Normal Range |
|-------------------------|-------------------|-------------------|--------|------------------|
| Progesterone Metabolism | | | | |
| | b-Pregnanediol | Within range | 122.0 | ng/mg 40 - 300 |
| | a-Pregnanediol | Low end of range | 21.0 | ng/mg 15 - 110 |
| Androgen Metabolism | | | | |
| | DHEAS | Low end of range | 199.0 | ng/mg 60 - 2000 |
| | Androsterone | Within range | 1308.0 | ng/mg 640 - 3000 |
| | Etiocholanolone | High end of range | 1569.0 | ng/mg 460 - 1700 |
| | Testosterone | Within range | 74.2 | ng/mg 25 - 100 |
| | 5a-DHT | Below range | 7.9 | ng/mg 9 - 16.7 |
| | 5a-Androstanediol | Within range | 94.2 | ng/mg 49 - 147 |
| | 5b-Androstanediol | Within range | 71.7 | ng/mg 30 - 147 |
| | Epi-Testosterone | High end of range | 89.9 | ng/mg 25 - 100 |
| Estrogen Metabolites | | | | |
| | Estrone(E1) | Within range | 7.0 | ng/mg 4 - 12 |
| | Estradiol(E2) | Within range | 0.8 | ng/mg 0.5 - 1.6 |
| | Estriol(E3) | Within range | 3.9 | ng/mg 2 - 6 |
| | 2-OH-E1 | Above range | 6.4 | ng/mg 0 - 3 |
| | 4-OH-E1 | Above range | 0.9 | ng/mg 0 - 0.5 |
| | 16-OH-E1 | High end of range | 0.7 | ng/mg 0 - 0.8 |
| | 2-Methoxy-E1 | Above range | 3.6 | ng/mg 0 - 2 |
| | 2-OH-E2 | Within range | 0.27 | ng/mg 0 - 0.5 |

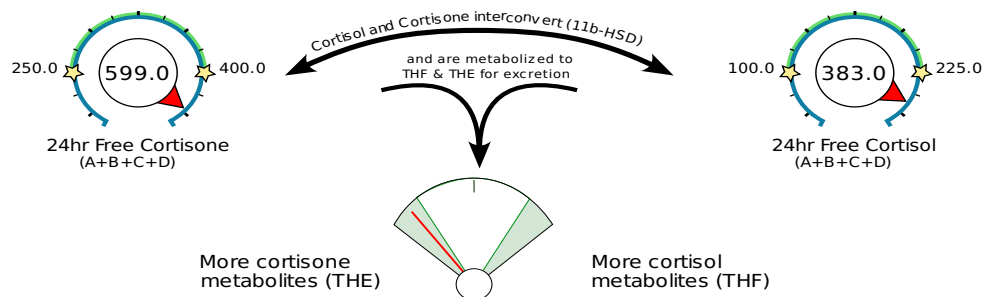
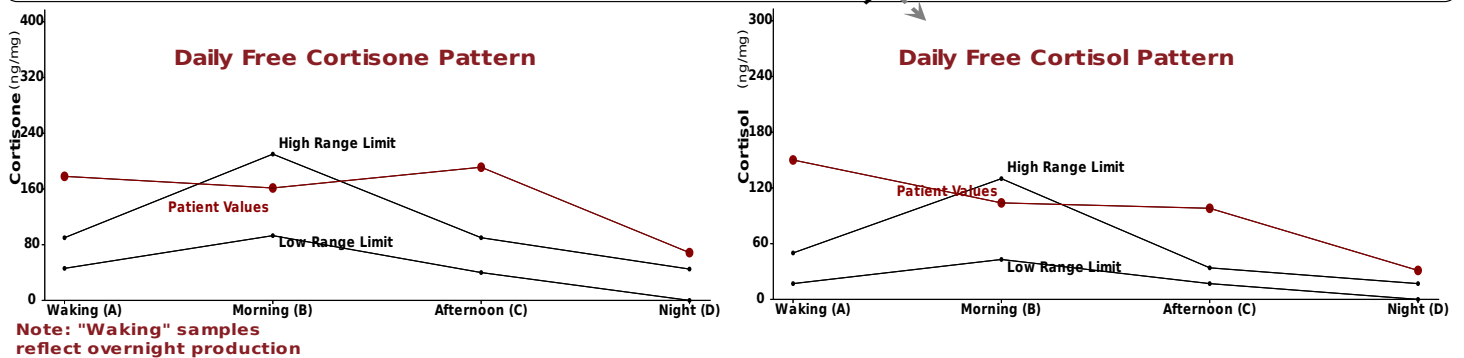
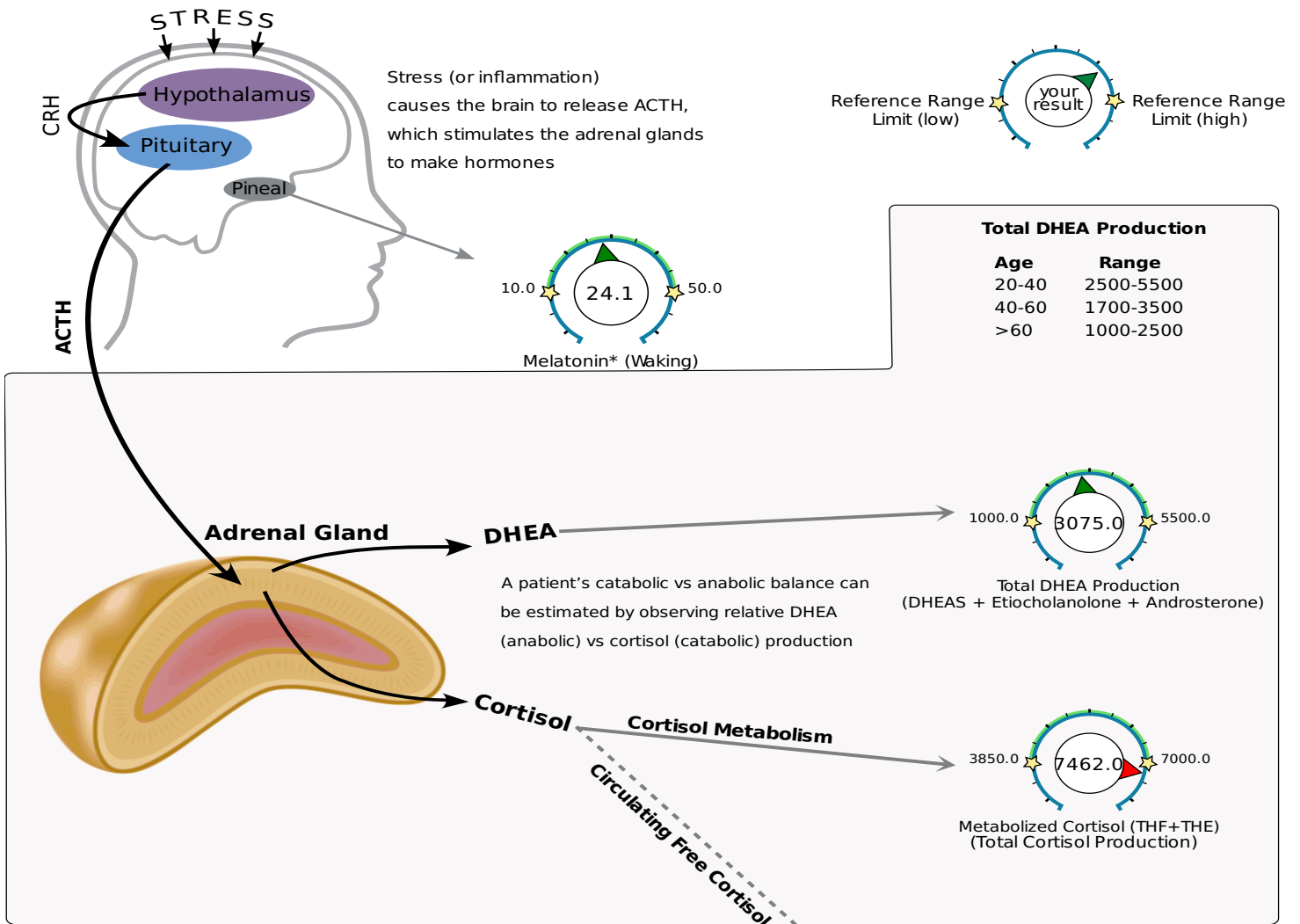
HOW TO READ YOUR RESULTS: Hormones are presented on this page graphically in the order the body metabolizes them. Arrows represent conversion from one hormone to another. The stars represent the low and high limits of the reference ranges (see example, right). The number in the middle is your result.



Collection Times:

2016-03-07 06:30PM
2016-03-07 11:30PM
2016-03-08 02:30AM
2016-03-08 10:30AM
2016-03-08 12:50PM

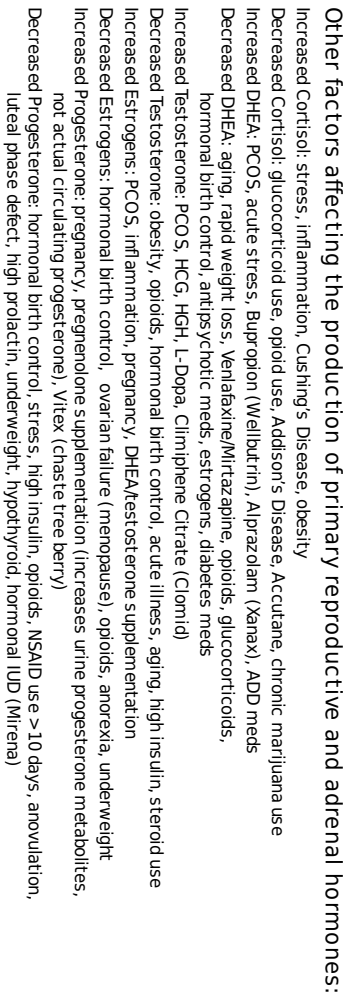
| Category | Test | | Result | Units | Normal Range |
|--|--------------------------------|------------------|--------|-------|--------------|
| Creatinine | | | | | |
| | Creatinine A (Waking) | Below range | 0.23 | mg/ml | 0.3 - 3 |
| | Creatinine B (Morning) | Within range | 1.37 | mg/ml | 0.3 - 3 |
| | Creatinine C (Afternoon) | Below range | 0.25 | mg/ml | 0.3 - 3 |
| | Creatinine D (Night) | Below range | 0.26 | mg/ml | 0.3 - 3 |
| Daily Free Cortisol and Cortisone | | | | | |
| | Cortisol A (Waking) | Above range | 150.1 | ng/mg | 17 - 50 |
| | Cortisol B (Morning) | Within range | 103.9 | ng/mg | 43 - 130 |
| | Cortisol C (Afternoon) | Above range | 98.1 | ng/mg | 17 - 34 |
| | Cortisol D (Night) | Above range | 31.2 | ng/mg | 0 - 17 |
| | Cortisone A (Waking) | Above range | 178.1 | ng/mg | 46 - 90 |
| | Cortisone B (Morning) | Within range | 161.4 | ng/mg | 93 - 210 |
| | Cortisone C (Afternoon) | Above range | 191.2 | ng/mg | 40 - 90 |
| | Cortisone D (Night) | Above range | 68.6 | ng/mg | 0 - 45 |
| | 24hr Free Cortisol | Above range | 383.0 | ug | 100 - 225 |
| | 24hr Free Cortisone | Above range | 599.0 | ug | 250 - 400 |
| Cortisol Metabolites and DHEAS | | | | | |
| | a-Tetrahydrocortisol (a-THF) | Below range | 95.0 | ng/mg | 220 - 720 |
| | b-Tetrahydrocortisol (b-THF) | Above range | 2435.0 | ng/mg | 1330 - 2330 |
| | b-Tetrahydrocortisone (b-THE) | Above range | 4932.0 | ng/mg | 2100 - 4000 |
| | Metabolized Cortisol (THF+THE) | Above range | 7462.0 | ng/mg | 3850 - 7000 |
| | DHEAS | Low end of range | 199.0 | ng/mg | 60 - 2000 |
| Melatonin (*measured as 6-OH-Melatonin-Sulfate) | | | | | |
| | Melatonin* (Waking) | Within range | 24.1 | ng/mg | 10 - 50 |





dutch
Driedu in d'Estor Compagnie sive ormon es

Page 6 of 8
CLIA Lic. #38D2047310
DutchTest.com



Provider Notes

Thank you for testing with us! If this is your first report, you are encouraged to watch our educational videos on how to read the report. There are hyperlinks to these videos on the first page of a DUTCH Complete or in these comments (below). The videos can also be seen by going to www.DutchTest.com and visiting the video library. Comments in the report that are specific to the patient ARE IN ALL CAPS. The other information is general information that we hope you will find useful in understanding the patient's results. Reference ranges updated 7/23/2015.

THE PATIENT IS EXPERIENCING SIGNIFICANT FATIGUE IN THE MORNINGS

THE PATIENT HAS AT LEAST ONE CREATININE VALUE THAT IS VERY LOW. ALL TEST VALUES ARE DIVIDED BY CREATININE TO CORRECT FOR HYDRATION, BUT THIS RELATIONSHIP HAS LIMITS. AS CREATININE GETS TOO LOW, ACCURACY MAY BE SLIGHTLY COMPROMISED. THIS HAPPENS MOST COMMONLY WHEN THE PATIENT DOES NOT HEED THE INSTRUCTIONS AND CONSUMES EXCESSIVE FLUIDS DURING COLLECTION. IF THIS IS TRUE OF ONE OR TWO SAMPLES ONLY, CORTISOL AND CORTISONE MAY BE EFFECTED AT THE TIME OF THOSE SAMPLES. IF IT IS TRUE OF MOST OR ALL OF THE SAMPLES, ALL RESULTS MAY BE SOMEWHAT AFFECTED. FOR THIS REASON THE INSTRUCTIONS ADVISE PATIENTS TO AVOID EXCESSIVE FLUIDS LEADING UP TO AND AT THE TIME OF TESTING. IF THE PATIENT IS ACTUALLY EXCRETING LESS CREATININE THAN THEY SHOULD (FOR A MEDICAL REASON) THIS WILL ALSO CAUSE THE ENTIRE HORMONE PANEL TO BE ELEVATED DUE TO THE OVERALL LOW CREATININE IN THE CALCULATION. OUR EXPERIENCE IS THAT MALE VALUES LESS THAN 0.2mg/mL AND FEMALE VALUES LESS THAN 0.1 MAY BE PROBLEMATIC FOR THE INDIVIDUAL VALUES FROM THOSE SPECIFIC SAMPLES WITH LOW CREATININE VALUES.

Androgen Metabolism: Testosterone is made in the testis and the adrenal glands however in men the adrenal production is a somewhat insignificant fraction. a-DHT (a-dihydrotestosterone) is the most potent androgen (3X more than testosterone), but it is primarily made within the liver and target cells (it is a paracrine hormone) and not by the gonads. a-DHT is subsequently deactivated to a-androstenediol within target tissues and then conjugated (glucuronidation) for excretion. As such, a-androstenediol may better represent a-DHT even though its metabolic precursor is more biologically active and well known however we do report both on the test. Only a fraction of a-DHT formed actually enters circulation as a-DHT (Toscano, 1987). The corresponding beta metabolites (for example b-DHT) are not androgenic.

Androgens help to promote proper sexual desire and function, and generally contribute to attributes that are typically more pronounced in males than females (general and sexual aggression, muscle mass, increased facial/body hair, reduction of fat deposition, etc). As males age, they make less testosterone. Androgens are turned into estrogens (for men and women) so assessing metabolism also includes looking at estrogen levels.

5a-Reductase Activity: The competing enzymes 5a and 5b-reductase act on the androgens androstenedione (creating androsterone and etiocholanolone located under the progesterone picture) and testosterone (creating a-DHT and b-DHT). They also metabolize progesterone, and cortisol. The alpha metabolites of androstenedione and testosterone are far more androgenic than their beta counterparts. Consequently, increased 5a-reductase activity may be accompanied by clinical signs of androgenicity (excess facial hair growth, scalp hair loss, acne, irritability, oily skin, prostate issues in men...etc). If the patient heavily favors the 5a pathway and there are concerns of excess androgenicity (or prostate cancer risk), this may be worth addressing.

Estrogen Metabolism: While usually considered "female" hormones, estrogens are present in males also. In men elevated estrogen levels have been associated with weight gain, breast development, mood swings, cardiovascular and prostate problems. The primary concern for male patients is if they are making too much. Estrogens are produced from androstenedione and testosterone via a process called aromatization.

Most estrogen is metabolized down into the healthier 2-OH pathway. These 2-OH metabolites are considered protective in women (from breast cancer) but this is also true of men with respect to prostate cancer. It is ideal if the 2-OH pathway (from the 2nd pie chart) is heavily favored over the more potent 16-OH estrogens or the carcinogenic 4-OH estrogens. It is our position that the ratio of 2:16 OHE1 is not as relevant as has been thought historically (Obi, 2011). Providers may still wish to use this index and it can be calculated by simply dividing the two numbers. A male reference range for the ratio with our methodology is 2.6-6.6.

The methylation activity gauge shows how effectively the body makes methoxy estrogens from hydroxyestrogens. Normal or high methylation activity is important in protecting the body from the harmful 4-OH estrogens made in phase 1 detoxification.

Progesterone levels are of marginal value in men, although deficiency can be associated with some clinical conditions such as depression, fatigue, and low libido.

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 represents overall production of cortisol therefore both should be taken into account to correctly assess adrenal function.

The Daily Free Cortisol Pattern: In healthy adrenal function, cortisol levels are expected to rise in the early morning and fall throughout the day, reaching the lowest point around 1am and peaking 30-60min after waking. The waking sample represents the total of free cortisol throughout the sleeping period. Cortisone is the inactive form of cortisol. Its pattern is of secondary importance, but at times can give additional clarity and is provided on the adrenal page. Typical urine testing (24-hour collection) averages the daily production of cortisol. This approach is not able to properly characterize individuals whose cortisol patterns do not fit the typical rise then fall pattern through the day. Dysfunctional diurnal patterns have been associated with health-related problems such as fatigue and insomnia.

The daily total of free cortisol is approximated by summing the four measurements. This calculated value correlates to a 24-hour free cortisol value. It is helpful to compare the relative level of 24-hr free cortisol with metabolized cortisol to understand HPA-axis activity. The total of free cortisol for the day only represents about 1-3% of the total production. The total of the metabolites is a better marker for overall cortisol production.

BOTH FREE AND METABOLIZED CORTISOL LEVELS ARE ELEVATED. THIS PATIENT'S HPA-AXIS APPEARS TO BE OVERACTIVE AND EFFORTS TO CALM (AND SUPPORT) ADRENAL FUNCTION IS LIKELY ADVISABLE.

The Cortisol-Cortisone Balance: Cortisol, which is the active hormone, can convert into cortisone, the inactive form. They convert back and forth in different parts of the body. We tell which one you make more of by looking at whether cortisol metabolites (aTHF, bTHF) or cortisone metabolites (bTHE) are made more (compared to what is normal) in the gauge at the bottom of the adrenal page. The deactivation of cortisol to cortisone (via enzyme 11b-HSD II) occurs predominantly in the kidneys, colon, and saliva glands. The local formation of inactive cortisone from cortisol in the kidney is strongly reflected in urine. Activation of cortisone to cortisol takes place primarily in the liver, adipose tissue, gonads, brain, and muscle. Within these same tissues (mostly the liver) the free hormones are also converted to their metabolites (cortisol to a/b-THF, cortisone to THE). Balance between the two is usually preferred, but making more cortisol than cortisone is sometimes good to help give you enough cortisol if your levels are low however a preference for the active cortisol is enhanced by central adiposity, hypothyroidism, inflammation, and supplements such as licorice root extract. Cortisone formation is enhanced by growth hormone, estrogen, coffee and hyperthyroidism.

Reading the Report: The first page of the Dutch Complete lab report is a summary page while the second page of the Dutch Complete lab report and first page of the Dutch sex hormone and Dutch adrenal test are a classic lab report showing each result and the respective range of each hormone. Reference ranges shown are those of young healthy individuals. The graphical representation of results on the page that follows allows the viewing of hormone results within the biochemical flowchart to more easily see the relative level of each hormone. The gauge format shows the patient result (represented by the "needle" of the gauge) and the area between the stars represents the reference range. Reference ranges are typically set at the 20th to the 80th percentile of young, healthy individuals (DHEAS for example). This means that a result at the low end of a range is lower than 80 percent of young, healthy individuals. Likewise a result at the high end of a range is higher than 80 percent of the population. Some reference ranges are set more widely. For example, slightly elevated progesterone is not generally considered problematic, so its metabolites have reference ranges that extend further (90th percentile instead of 80th).

The "fan" style gauges are used for indexes/ratios such as on 5a-reductase activity, cortisol/cortisone, and estrogen methylation. Because these values are all based on ratios there are no values or units, but they give a general idea of a particular relationship and can tell you how 'turned up' or 'turned down' a particular process is. The middle of the gauge represents an average value, while the lines towards the edge represent results lower or higher than most (80%) of the population. Being outside of any range is not always considered unfavorable. For example, on the estrogen methylation gauge an elevated level means someone methylates estrogens very effectively which may have positive consequences.

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 well 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.