Accession # 00280402
Male Sample Report
123 A Street
Sometown , CA 90266

Ordering Physician:
Precision Analytical

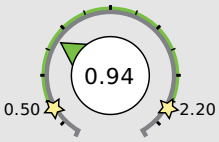
DOB: 1966-05-06
Age: 50
Gender: Male

Collection Times:
2016-10-01 06:01AM
2016-10-01 08:01AM
2016-10-01 06:01PM
2016-10-01 10:01PM

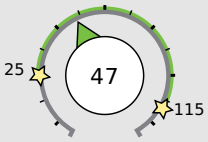
Hormone Testing Summary

Key (how to read the results):

Sex Hormones



Estradiol(E2)



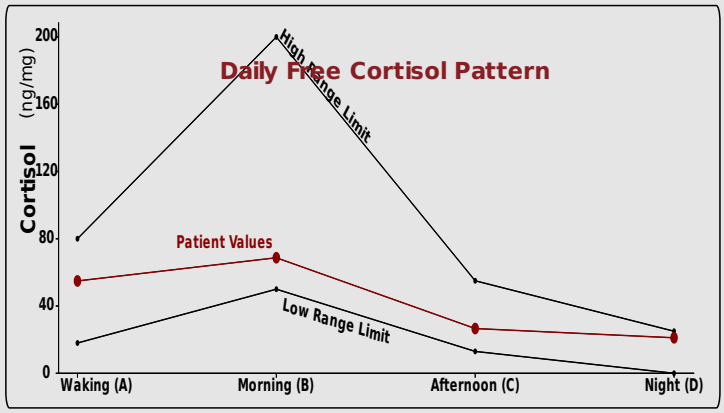
Testosterone

Testosterone

Age	Range
18-25	50-115
26-40	40-95
41-60	30-80
>60	25-60

Adrenal Hormones

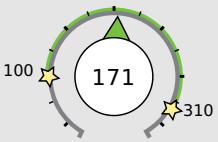
See pages 4 and 5 for a more complete breakdown of adrenal hormones



Total DHEA Production

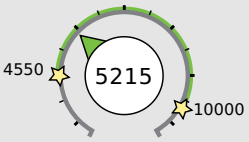
Age	Range
20-39	3000-5500
40-60	2000-4000
>60	1000-2500

Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)



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

cortisol metabolism



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

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

The following videos (which can also be found on the website under the listed names along with others) may aid your understanding:
DUTCH Complete Overview | Estrogen Tutorial | Male Androgen Tutorial | Cortisol Tutorial

PLEASE BE SURE TO READ BELOW FOR ANY SPECIFIC LAB COMMENTS. More detailed comments can be found on page 8.

Accession # 00280402
Male Sample Report
123 A Street
Sometown , CA 90266

Sex Hormones and Metabolites

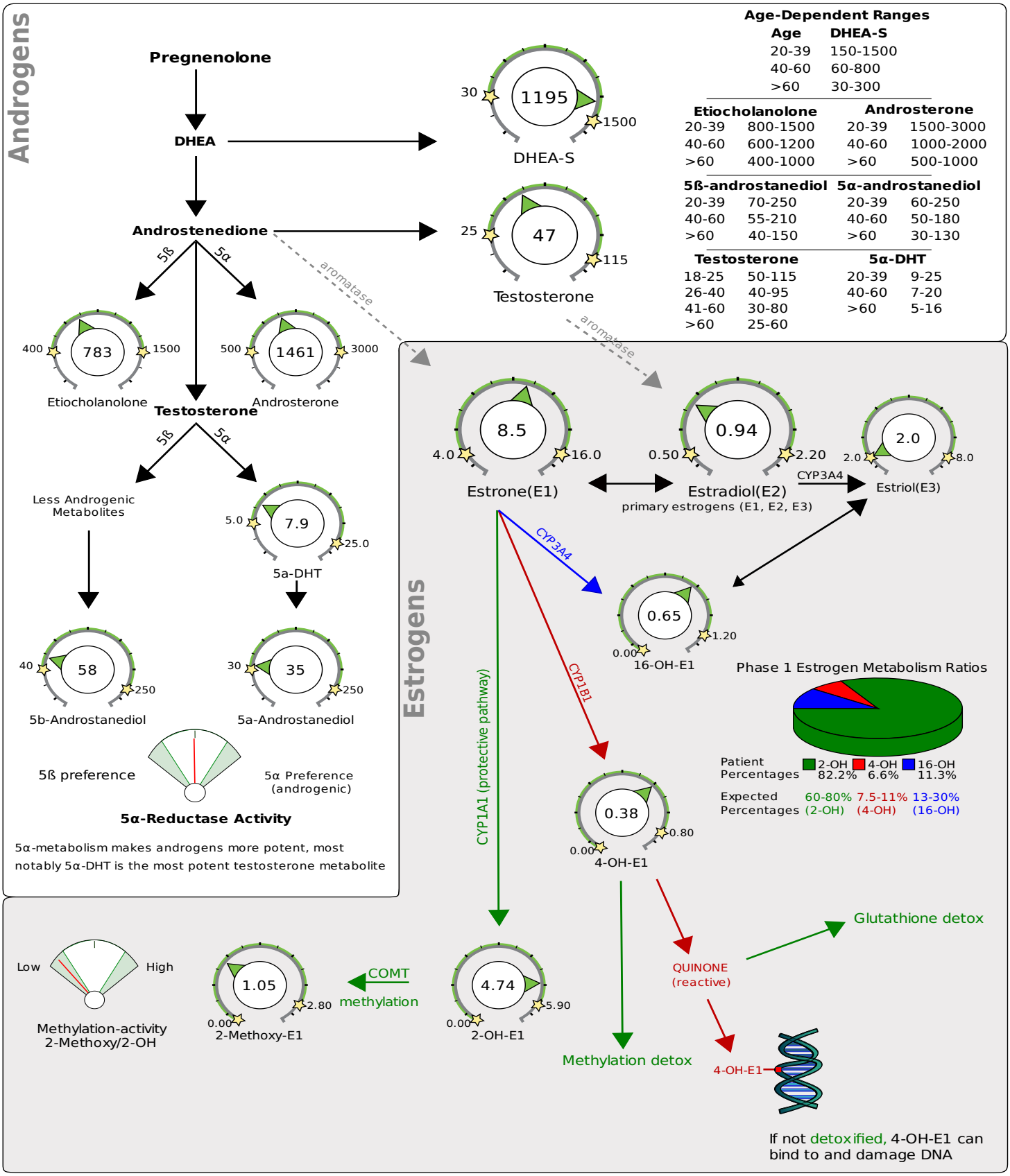
Ordering Physician:
Precision Analytical

DOB: 1966-05-06
Age: 50
Gender: Male

Collection Times:
2016-10-01 06:01AM
2016-10-01 08:01AM
2016-10-01 06:01PM
2016-10-01 10:01PM

Category	Test		Result	Units	Normal Range
Progesterone Metabolites (Urine)					
	b-Pregnanediol	Low end of range	107.0	ng/mg	75 - 400
	a-Pregnanediol	Low end of range	40.0	ng/mg	20 - 130
Estrogens and Metabolites (Urine)					
	Estrone(E1)	Within range	8.5	ng/mg	4 - 16
	Estradiol(E2)	Within range	0.94	ng/mg	0.5 - 2.2
	Estriol(E3)	Low end of range	2.0	ng/mg	2 - 8
	2-OH-E1	High end of range	4.74	ng/mg	0 - 5.9
	4-OH-E1	Within range	0.38	ng/mg	0 - 0.8
	16-OH-E1	Within range	0.65	ng/mg	0 - 1.2
	2-Methoxy-E1	Within range	1.05	ng/mg	0 - 2.8
	2-OH-E2	Within range	0.28	ng/mg	0 - 0.6
	4-OH-E2	Within range	0.1	ng/mg	0 - 0.3
	2-Methoxy-E2	Within range	0.5	ng/mg	0 - 0.8
	Total Estrogen	Within range	19.2	ng/mg	10 - 34
Androgens and Metabolites (Urine)					
	DHEA-S	Within range	1195.0	ng/mg	30 - 1500
	Androsterone	Within range	1461.0	ng/mg	500 - 3000
	Etiocholanolone	Within range	783.0	ng/mg	400 - 1500
	Testosterone	Within range	46.8	ng/mg	25 - 115
	5a-DHT	Low end of range	7.9	ng/mg	5 - 25
	5a-Androstanediol	Low end of range	35.4	ng/mg	30 - 250
	5b-Androstanediol	Low end of range	57.7	ng/mg	40 - 250
	Epi-Testosterone	Low end of range	35.6	ng/mg	25 - 115

Hormone metabolite results from the previous page are presented here as they are found in the steroid cascade. See the Provider Comments for more information on how to read the results.



Accession # 00280402
Male Sample Report
123 A Street
Sometown , CA 90266

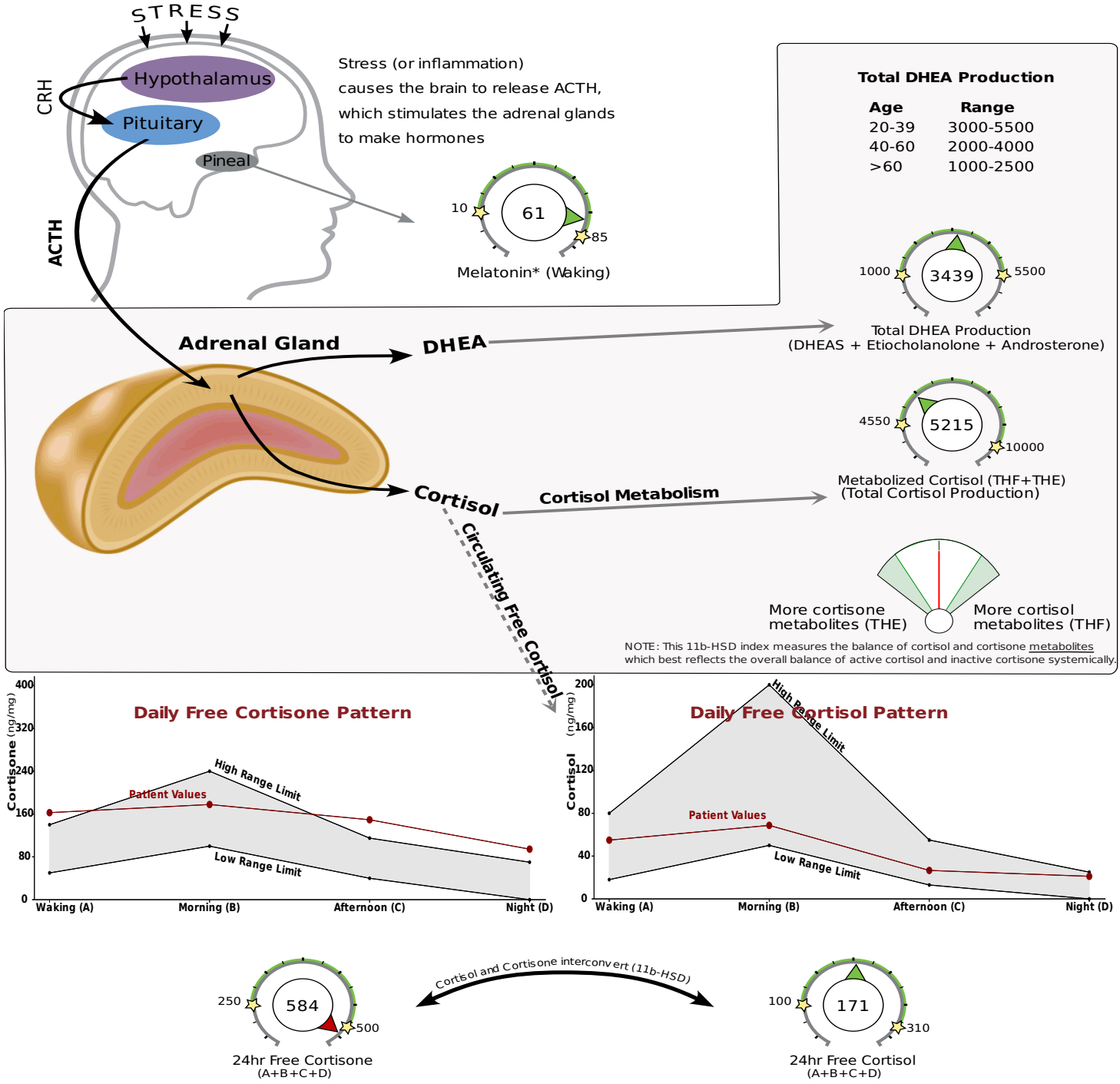
Adrenal

Ordering Physician:
Precision Analytical

DOB: 1966-05-06
Age: 50
Gender: Male

Collection Times:
2016-10-01 06:01AM
2016-10-01 08:01AM
2016-10-01 06:01PM
2016-10-01 10:01PM

Category	Test		Result	Units	Normal Range
Creatinine (Urine)					
	Creatinine A (Waking)	Within range	1.1	mg/ml	0.3 - 3
	Creatinine B (Morning)	Within range	0.93	mg/ml	0.3 - 3
	Creatinine C (Afternoon)	Within range	0.9	mg/ml	0.3 - 3
	Creatinine D (Night)	Within range	1.13	mg/ml	0.3 - 3
Daily Free Cortisol and Cortisone (Urine)					
	Cortisol A (Waking)	Within range	54.9	ng/mg	18 - 80
	Cortisol B (Morning)	Low end of range	68.7	ng/mg	50 - 200
	Cortisol C (Afternoon)	Within range	26.6	ng/mg	13 - 55
	Cortisol D (Night)	High end of range	21.1	ng/mg	0 - 25
	Cortisone A (Waking)	Above range	162.6	ng/mg	50 - 140
	Cortisone B (Morning)	Within range	177.8	ng/mg	100 - 240
	Cortisone C (Afternoon)	Above range	149.3	ng/mg	40 - 115
	Cortisone D (Night)	Above range	94.4	ng/mg	0 - 70
	24hr Free Cortisol	Within range	171.3	ng/mg	100 - 310
	24hr Free Cortisone	Above range	584.0	ng/mg	250 - 500
Cortisol Metabolites and DHEA-S (Urine)					
	a-Tetrahydrocortisol (a-THF)	Within range	419.0	ng/mg	175 - 700
	b-Tetrahydrocortisol (b-THF)	Low end of range	1961.0	ng/mg	1750 - 4000
	b-Tetrahydrocortisone (b-THE)	Low end of range	2835.0	ng/mg	2350 - 5800
	Metabolized Cortisol (THF+THE)	Low end of range	5215.0	ng/mg	4550 - 10000
	DHEA-S	Within range	1195.0	ng/mg	30 - 1500



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 9.9ng/mg.
The waking "A2" sample registered a cortisol value of 87.1ng/mg.
These two values are averaged together, taking into account the amount of time each one represents, to create the "A" value of approximately 54.9ng/mg that you will see on the report.
In this particular case, this A2 value is larger than the sample (collected two hours after waking) expected to have the highest cortisol value. Cortisol levels typically rise sharply *after* waking thanks to the cortisol awakening response. In a case like this where the waking sample (A2) shows higher levels, this cortisol awakening response may have happened while the patient was in bed before rising.

Accession # 00280402
Male Sample Report
123 A Street
Sometown , CA 90266

Organic Acid Tests (OATs)

Ordering Physician:
Precision Analytical

DOB: 1966-05-06
Age: 50
Gender: Male

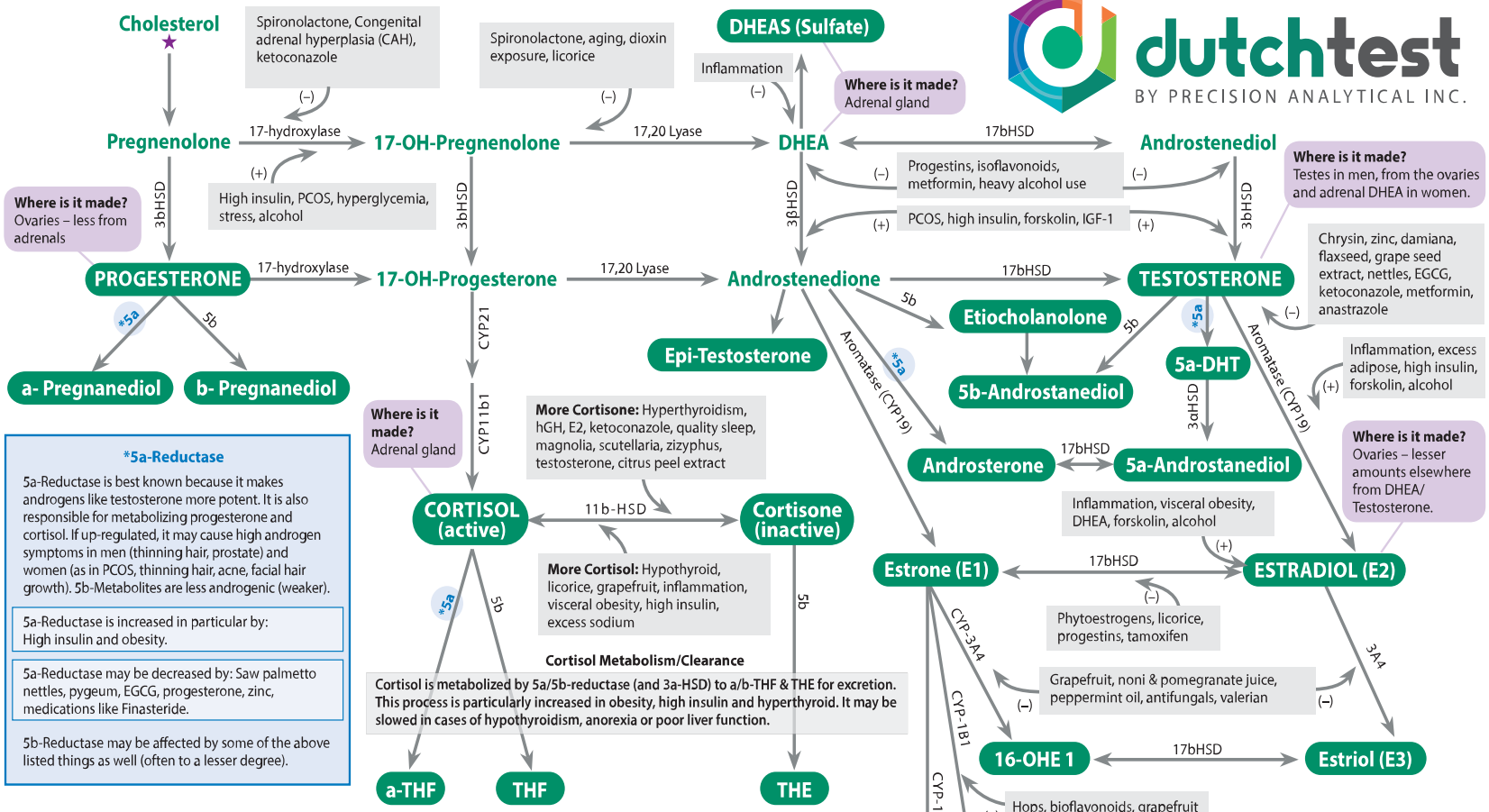
Collection Times:
2016-10-01 06:01AM
2016-10-01 08:01AM
2016-10-01 06:01PM
2016-10-01 10:01PM

Category	Test		Result	Units	Normal Range
Nutritional Organic Acids					
Vitamin B12 Marker (may be deficient if high) - (Urine)					
	Methylmalonate (MMA)	Within range	1.4	ug/mg	0 - 3
Vitamin B6 Markers (may be deficient if high) - (Urine)					
	Xanthurenate	Within range	0.8	ug/mg	0 - 2.1
	Kynurenate	Within range	3.5	ug/mg	0 - 9.3
Glutathione Marker (may be deficient if low or high) - (Urine)					
	Pyroglutamate	Low end of range	44.1	ug/mg	43 - 85
Neurotransmitter Metabolites					
Dopamine Metabolite - (Urine)					
	Homovanillate (HVA)	Low end of range	5.3	ug/mg	4.8 - 19
Norepinephrine/Epinephrine Metabolite - (Urine)					
	Vanilmandelate (VMA)	Low end of range	3.1	ug/mg	2.8 - 8
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)					
	Melatonin* (Waking)	Within range	61.2	ng/mg	10 - 85
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)					
	8-OHdG (Waking)	Within range	2.8	ng/mg	0 - 8.8

Steroid Pathways

Find these Hormones on the DUTCH Complete

Primary hormones (in CAPS) are made by organs by taking up cholesterol ★ and converting it locally to, for example, progesterone. Much less is made from circulating precursors like pregnenolone. For example, taking DHEA can create testosterone and estrogen, but far less than is made by the testes or ovaries, respectively.



*5a-Reductase

5a-Reductase is best known because it makes androgens like testosterone more potent. It is also responsible for metabolizing progesterone and cortisol. If up-regulated, it may cause high androgen symptoms in men (thinning hair, prostate) and women (as in PCOS, thinning hair, acne, facial hair growth). 5b-Metabolites are less androgenic (weaker).

5a-Reductase is increased in particular by: High insulin and obesity.

5a-Reductase may be decreased by: Saw palmetto nettles, pygeum, EGCG, progesterone, zinc, medications like Finasteride.

5b-Reductase may be affected by some of the above listed things as well (often to a lesser degree).

Other factors affecting the production of primary reproductive and adrenal hormones:

- Increased Cortisol: stress, inflammation, Cushing's Disease, obesity
- Decreased Cortisol: glucocorticoid use, opioid use, Addison's Disease, Accutane, chronic marijuana use
- Increased DHEA: PCOS, acute stress, Bupropion (Wellbutrin), Alprazolam (Xanax), ADD meds
- Decreased DHEA: aging, rapid weight loss, Venlafaxine/Mirtazapine, opioids, glucocorticoids, hormonal birth control, antipsychotic meds, estrogens, diabetes meds
- Increased Testosterone: PCOS, HCG, HGH, L-Dopa, Climiphene Citrate (Clomid)
- Decreased Testosterone: obesity, opioids, hormonal birth control, acute illness, aging, high insulin, steroid use
- Increased Estrogens: PCOS, inflammation, pregnancy, DHEA/testosterone supplementation
- Decreased Estrogens: hormonal birth control, ovarian failure (menopause), opioids, anorexia, underweight
- Increased Progesterone: pregnancy, pregnenolone supplementation (increases urine progesterone metabolites, not actual circulating progesterone), Vitex (chaste tree berry)
- Decreased Progesterone: hormonal birth control, stress, high insulin, opioids, NSAID use >10 days, anovulation, luteal phase defect, high prolactin, underweight, hypothyroid, hormonal IUD (Mirena)

Information on this chart is for educational purposes only and is not a suggestion for supplementation with any of the listed items. References available upon request.

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Male Sample Report
FINAL REPORT
01/04/2019

Precision Analytical (Raymond Grimsbo, Lab Director)
3138 Rivergate Street #301C
McMinnville, OR 97128

Provider Notes

How to read the DUTCH report

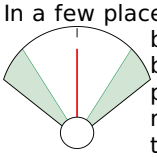
This report is not intended to treat, cure or diagnose any specific diseases. The graphic dutch dials in this report are intended for quick and easy evaluation of which hormones are out of range. Results below the left star are shaded yellow and are below range (left). Results between the stars and shaded 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.

Low Example

Normal Example

High Example

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 cortisone 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**.

Note: The dates listed on the samples imply that they were older than our allowed 3 weeks when they were received. The instructions ask that patients freeze or refrigerate samples if they are to be held. If that is not the case, the free cortisol and cortisone levels may drop somewhat over time if the samples are too old. Other hormones tested are stable for more than 12 weeks at room temperature. Samples that are refrigerated or frozen are stable for months.

Androgen Metabolism

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

- **The status (low, normal or high?) of DHEA:**

DHEA and androstenedione are made almost exclusively by the adrenal gland (although a smaller amount is made in the ovaries). These hormones appear in urine as DHEA-S (DHEA-Sulfate), androsterone and etiocholanolone. The best way to assess the total production of DHEA is to add up these three metabolites. This total can be seen on the first page of the DUTCH Complete (and DUTCH Plus). DHEA production decreases quite significantly with age. Age-dependent ranges can be seen on the graphical page of results.

The Total DHEA Production (page 1) was about 3,439ng/mg which is within the overall range and also within the age-dependent range for this patient. This implies that the adrenal glands are producing appropriate DHEA levels.

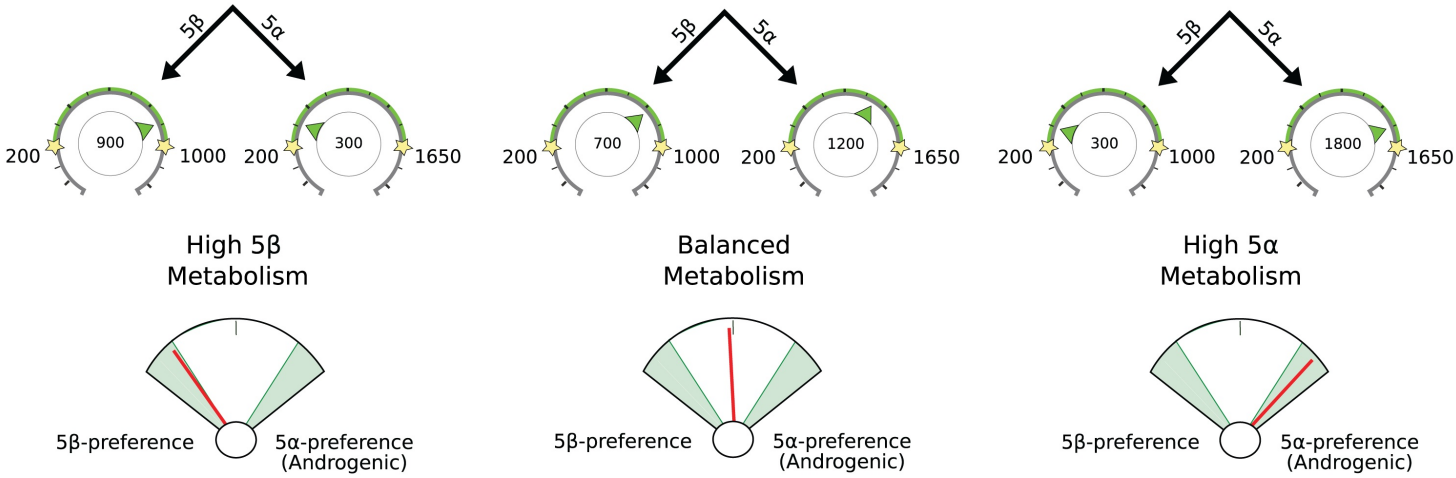
- **The status (low, normal or high?) of testosterone:**

The testes make most of the male's testosterone. Levels tend to be their highest at around 20 years of age and start to decline when men get into their 30's. Levels continue to drop as men age. Consider the appropriate age-dependent range for your patient. In older men, you can also consider the 18-25 year-old group to approximate what levels may have been when the patient was young and relatively healthy.

- **The metabolic preference for the 5a (5-alpha) or 5b (5-beta) pathway:**

5a-reductase converts testosterone into 5a-DHT (DHT), which is even more potent (~3x) than testosterone. High levels of DHT can lead to symptoms associated with too much testosterone (thinning scalp hair, acne, etc.) and may also be associated with prostate issues in older men. Metabolites created down the 5b-pathway are significantly less androgenic than their 5a counterparts. In the examples below, the example on the left shows a patient with 5b-metabolism preference. A patient with a pattern like the example on the right may have high androgen symptoms even though testosterone is in the normal range because of the likely preference for turning a lot of his testosterone into DHT. The fan-style gauge below the hormones shows the 5a or 5b preference based on the balance between etiocholanolone (5b) and androsterone (5a) as well as 5a-androstanediol and 5b-androstanediol.

Example of how to read fan-style gauge for 5a-reductase activity:



You will also see levels of epi-testosterone, which is not androgenic like testosterone. It happens to be produced in about the same concentrations as testosterone (this is an approximate relationship). This can be helpful to assess testosterone therapy and rare cases where testosterone may have other complexities.

Estrogen Metabolism

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

- **The status (low, normal or high?) of estrogen production:**

Levels of the primary estrogen, estradiol (the strongest estrogen), as well as "total estrogens" may be considered.

- **Phase I Metabolism:**

Estrogen is metabolized (primarily by the liver) down three phase I pathways. The 2-OH pathway is considered the safest because of the anti-cancer properties of 2-OH metabolites. Conversely, the 4-OH pathway is considered the most genotoxic as its metabolites can create reactive products that damage DNA. The third pathway, 16-OH creates the most estrogenic of the metabolites (although still considerably less estrogenic than estradiol) - 16-OH-E1.

When evaluating phase I metabolism, it may be important to look at the ratios of the three metabolites to see which pathways are preferred relative to one another. It may also be important to compare these metabolites to the levels of the parent hormones (E1, E2). If the ratios of the three metabolites are favorable but overall levels of metabolites are much lower than E1 and E2, this may imply sluggish phase I clearance of estrogens, which can contribute to high levels of E1 and E2.

The pie chart will assist you in comparing the three pathway options of phase I metabolism compared to what is "normal." 2-OH metabolism can be increased by using products containing D.I.M. or I-3-C. These compounds are found (or created from) in cruciferous vegetables and are known for promoting this pathway.

- **Methylation (part of Phase II Metabolism) of estrogens:**

After phase I metabolism, both 4-OH and 2-OH (not 16-OH) estrogens can be deactivated and eliminated by methylation. The methylation-activity index shows the patient's ratio of 2-Methoxy-E1 / 2-OH-E1 compared to what is expected. Low methylation can be caused by low levels of nutrients needed for methylation and/or genetic abnormalities (COMT, MTHFR). The COMT enzyme responsible for methylation requires magnesium and methyl donors. Deficiencies in folate or vitamin B6 or B12 can cause low levels of methyl donors. MTHFR genetic defects can make it more difficult for patients to make sufficient methyl donors. Genetic defects in COMT can make methylation poor even in the presence of adequate methyl donors.

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

Progesterone metabolites have limited relevance in male patients, but may be worth considering in some patients with abnormal results. In this case, both progesterone metabolites are within the normal range.

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.

- **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.

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):**

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.

Nutritional Organic Acids

The following three organic acids are functional markers for vitamin deficiency. These compounds essentially back up in human biochemistry when a key nutrient is missing. These three metabolites have fairly straightforward interpretations. When the markers are elevated, it is likely that the patient's cellular levels of the related nutrient may be insufficient.

Methylmalonate (MMA)

Methylmalonate (also known as methylmalonic acid or MMA) is a functional marker of vitamin B12 (also known as cobalamin) deficiency. When cellular levels of B12 are low either from deficiency or due to a B12 transporter gene mutation, levels of MMA increase. This marker is considered superior to measuring serum B12 levels directly. A 2012 publication by Miller showed that 20% of those tested had a genetic defect in the protein that transports B12 to cells. These patients may have a functional B12 deficiency even if serum levels of B12 are normal.

If levels of MMA are elevated, it may be advisable to increase B12 consumption. Common foods high in B12 include beef liver, sardines, lamb, wild caught salmon, grass-fed beef, nutritional yeast and eggs. Vitamin B12 levels can also be increased through supplementation of B12 (taken as cobalamin, methylcobalamin, hydroxycobalamin, or adenosylcobalamin). Symptoms of a vitamin B12 deficiency include: fatigue, brain fog, memory problems, muscle weakness, unsteady gait, numbness, tingling, depression, migraines/headaches and low blood pressure.

Xanthurenate

Xanthurenate (also known as xanthurenic acid) and Kynurenate (kynurenic acid) are functional markers of vitamin B6 (also known as pyridoxine) deficiency. Vitamin B6 is a critical co-factor to over 100 important reactions that occur in the human body and is stored in the highest concentrations in muscle tissue. Tryptophan is readily converted to NAD by the liver. One of the steps in this pathway requires B6. When there is insufficient B6, xanthurenate is made instead. Kynurenate may also become elevated when patients are B6 deficient because of a different, possibly less B6 dependent pathway. The pathways leading to these biomarkers have other influences, so they will not always agree. When Xanthurenate is elevated, Kynurenate is also elevated about 1/3 of the time. When both are elevated, a B6 deficiency is likely more certain and more severe.

Not only is xanthurenate an indicator of a lack of B6, it is also harmful to the human body. It complexes with insulin and decreases insulin sensitivity. In fact, rats fed xanthurenate will actually develop diabetes because of the effects on insulin. If xanthurenate levels are elevated, B6 supplementation may be considered. Food high in B6 include turkey breast, grass-fed beef, pinto beans, avocado, pistachios, chicken, sesame and sunflower seeds.

While there is always some tryptophan going down the kynurenine pathway towards NAD (and possibly xanthurenate), this process is up-regulated by inflammation, estrogen and cortisol. If levels of estrogen or cortisol are high, it may exacerbate xanthurenate elevations and increase the need for B6.

Xanthurenate can also bind to iron and create a complex that increases DNA oxidative damage resulting in higher 8-OHdG levels. If both markers are elevated, there is likely an antioxidant insufficiency.

Pyroglutamate

Pyroglutamate (also known as pyroglutamic acid) is a functional marker of glutathione deficiency. Pyroglutamate is a step in the production/recycling of glutathione. If the body cannot convert pyroglutamate forward, it will show up elevated in the urine. High pyroglutamate is an established marker for glutathione deficiency.

Glutathione is one of the most potent anti-oxidants in the human body. It is especially important in getting rid of toxins, including the reactive quinone species formed by 4-OH-E1 and 4-OH-E2. This reactive species can damage DNA if not detoxified by either methylation or glutathione.
Some have reported that low pyroglutamate may also be indicative of a need for glutathione; however, this is not established in the scientific literature.

Neurotransmitter Metabolites

The neurotransmitters dopamine, norepinephrine and serotonin are important for human health. Measuring neurotransmitters directly (direct testing of serotonin, for example) is difficult because of their instability and their urinary measurements are controversial with respect to how well they reflect the body's levels of these neuro-hormones. Each of these three neurotransmitters can be assessed indirectly by measuring their urine metabolites. While these metabolites are not a perfect reflection of what's going on in the brain, the scientific literature does affirm their use for a good representation of overall levels of these neurotransmitters.

Homovanillate (HVA)

Homovanillate (also known as HVA) is the primary metabolite of dopamine, a brain and adrenal neurotransmitter that comes from tyrosine (with BH4 and iron as co-factors) and goes on to create norepinephrine (noradrenaline) and epinephrine (adrenaline).
Low levels of HVA can be due to low levels of dopamine or poor conversion of dopamine to HVA. The latter may be due to insufficient levels of SAM, Magnesium, FAD and NAD which are needed to metabolize dopamine. Low circulating dopamine may be due to insufficient BH4, iron or tyrosine. It may also be seen when adrenal function is generally low. Low dopamine levels may be associated with addictions, cravings and pleasure seeking (to boost levels) in addition to sleepiness, impulsivity, tremors, less motivation, fatigue and low mood.
Elevated HVA may be caused by generally increased adrenal hormone output or because of a copper or vitamin C deficiency (which are needed for dopamine conversion to norepinephrine). Elevations may also be caused by a number of medications or supplements including: MAO inhibitors, quercetin, tyrosine, DL-phenylalanine (DLPA), L-dopa, macuna, dopamine medication (Levodopa, Sinemet, Methyldopa), SNRI medication (Wellbutrin), tricyclic antidepressants, amphetamines, appetite suppressants, and caffeine. Bananas also contain dopamine. Elevated dopamine may be associated with loss of memory, insomnia, agitation, hyperactivity, mania, hyper-focus, high stress and anxiety as well as addictions, cravings and pleasure seeking (to maintain high levels).

Vanilmandelate (VMA)

Vanilmandelate (also known as VMA) is the primary metabolite of norepinephrine and epinephrine (adrenaline). The adrenal gland makes cortisol and DHEA as well as norepinephrine and epinephrine. When adrenal hormone output is generally low, VMA levels may be low. If HVA levels are significantly higher than VMA, there may be a conversion problem from dopamine to norepinephrine. This case can be caused by a copper or vitamin C deficiency. The enzymes COMT (methylation) and MAO are needed to make VMA from norepinephrine. If these enzymes are not working properly, VMA may be low when circulating norepinephrine and/or epinephrine are not low. Low levels of norepinephrine and epinephrine may be associated with addictions, cravings, fatigue, low blood pressure, low muscle tone, intolerance to exercise, depression, loss of alertness.
When the body is under physical or psychological stress, VMA levels may increase. Because dopamine gets converted to norepinephrine and ultimately to VMA, the list of medications and supplements that increase HVA may also increase VMA. Elevated levels may be associated with feeling stressed, aggression, violence, impatience, anxiety, panic, worry, insomnia, paranoia, increased tingling/burning, loss of memory, pain sensitivity, high blood pressure and heart palpitations.
If VMA and HVA are both extremely high, it may be necessary to rule out a neuroblastic tumor.

Melatonin (measured as 6-OHMS)

Melatonin is not technically an adrenal or sex hormone however it is highly involved in the entire endocrine system. It is made in small amounts in the pineal gland in response to darkness and stimulated by Melanocyte Stimulating Hormone (MSH). A low MSH is associated with insomnia, an increased perception of pain, and mold exposure. Pineal melatonin (melatonin is also made in significant quantities in the gut) is associated with the circadian rhythm of all hormones (including female hormone release). It is also made in small amounts in the bone marrow, lymphocytes, epithelial cells and mast cells. Studies have shown that a urine sample collected upon waking has levels of 6-Hydroxymelatonin-sulfate (6-OHMS) that correlate well to the total levels of melatonin in blood samples taken continuously throughout the night. The DUTCH test uses the waking sample only to test levels of melatonin production.
Low melatonin levels may be associated with insomnia, poor immune response, constipation, weight gain or increased appetite. Elevated melatonin is usually caused by ingestion of melatonin through melatonin supplementation or eating melatonin-containing foods. Elevated melatonin production that is problematic is rare, but levels can be higher in patients with Chronic Fatigue Syndrome and may be phase shifted (peaking later) in some forms of depression.

8-OHdG (8-Hydroxy-2-deoxyguanosine)

8-OHdG (8-hydroxy-2-deoxyguanosine) results can be seen on page 6 of the DUTCH Complete (or DUTCH Plus) report. It is a marker for estimating DNA damage due to oxidative stress (ROS creation). 8-OHdG is considered pro-mutagenic as it is a biomarker for various cancer and degenerative disease initiation and promotion. It can be increased by chronic inflammation, increased cell turnover, chronic stress, hypertension, hyperglycemia/pre-diabetes/diabetes, kidney disease, IBD, chronic skin conditions (psoriasis/eczema), depression, atherosclerosis, chronic liver disease, Parkinson's (increasing levels with worsening stages), Diabetic neuropathy, COPD, bladder cancer, or insomnia. Studies have shown higher levels in patients with breast and prostate cancers. When levels are elevated it may be prudent to eliminate or reduce any causes and increase the consumption of antioxidant containing foods and/or supplements.
The reference range for 8-OHdG is a more aggressive range for Functional Medicine that puts the range limit at the 80th percentile for each gender. A classic range (average plus two standard deviations) would result in a range of 0-6ng/mg for

women and 0-10ng/mg for men. Seeking out the cause of oxidative stress may be more crucial if results exceed these limits.

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 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 12.20.2018)

	Low%	High%	Low	High		Low%	High%	Low	High
b-Pregnanediol	10%	90%	75	400	Cortisol A (waking)	20%	90%	18	80
a-Pregnanediol	10%	90%	20	130	Cortisol B (morning)	20%	90%	50	200
Estrone (E1)	10%	90%	4	16	Cortisol C (~5pm)	20%	90%	13	55
Estradiol (E2)	10%	90%	0.5	2.2	Cortisol D (bed)	20%	90%	0	25
Estriol (E3)	10%	90%	2	8	Cortisone A (waking)	20%	90%	50	140
2-OH-E1	0	90%	0	5.9	Cortisone B (morning)	20%	90%	100	240
4-OH-E1	0	90%	0	0.8	Cortisone C (~5pm)	20%	90%	40	115
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%	100	310
b-THE	20%	90%	2350	5800	24hr Free Cortisone	20%	90%	250	500

% = 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: