Accession # 00908319
Male Sample Report
123 A Street
Sometown, CA 90266

Sex Hormones and Metabolites

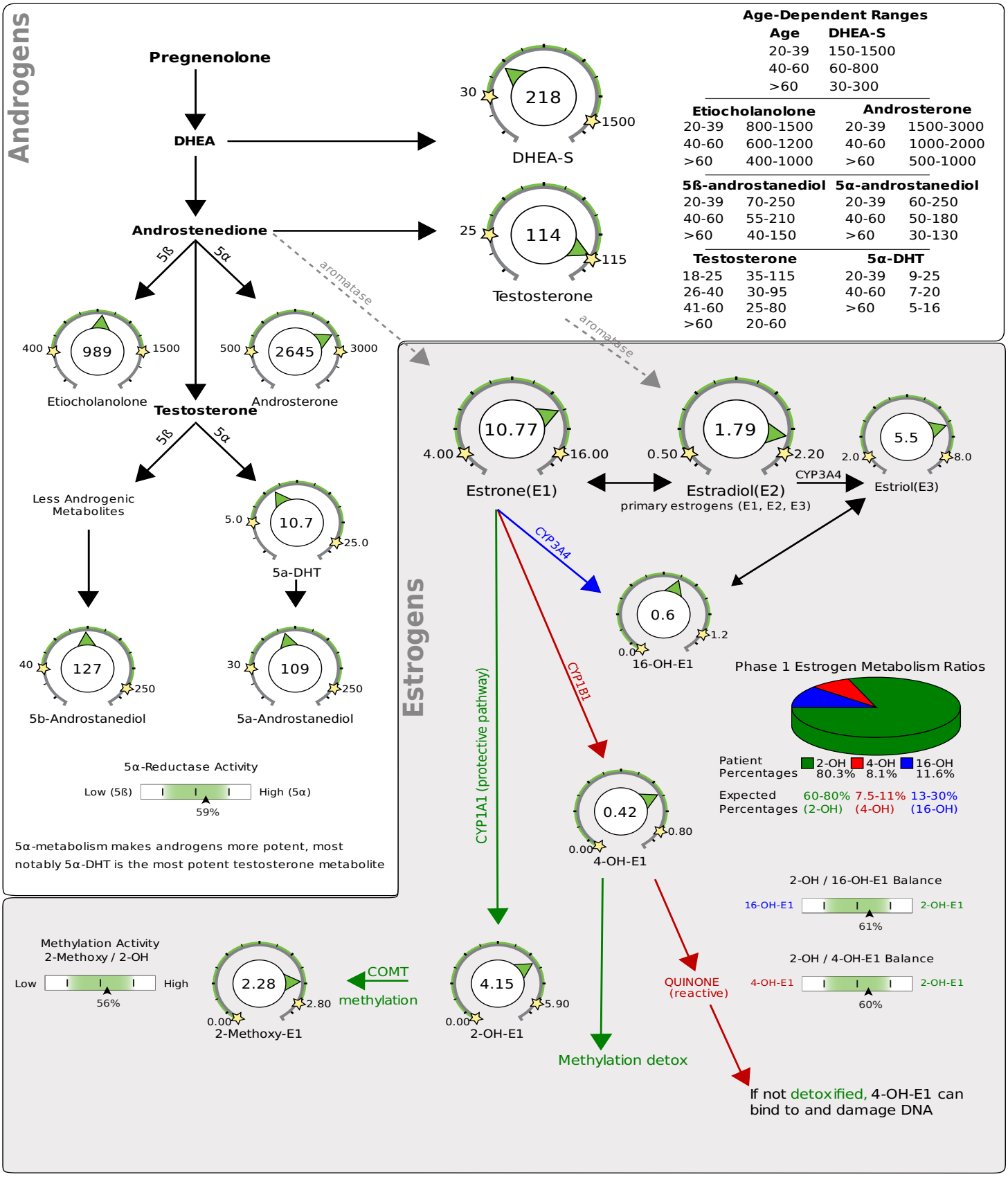
Ordering Provider:
Precision Analytical

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

Collection Times:
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
Progesterone Metabolites (Urine)					
	b-Pregnanediol	Within range	259.6	ng/mg	75 - 400
	a-Pregnanediol	Within range	117.5	ng/mg	20 - 130
Estrogens and Metabolites (Urine)					
	Estrone(E1)	Within range	10.77	ng/mg	4 - 16
	Estradiol(E2)	Within range	1.79	ng/mg	0.5 - 2.2
	Estriol(E3)	Within range	5.5	ng/mg	2 - 8
	2-OH-E1	Within range	4.15	ng/mg	0 - 5.9
	4-OH-E1	Within range	0.42	ng/mg	0 - 0.8
	16-OH-E1	Within range	0.6	ng/mg	0 - 1.2
	2-Methoxy-E1	Within range	2.28	ng/mg	0 - 2.8
	2-OH-E2	Within range	0.4	ng/mg	0 - 1.2
	4-OH-E2	Within range	0.13	ng/mg	0 - 0.25
	Total Estrogen	Within range	26.1	ng/mg	10 - 34
Metabolite Ratios					
	2-OH / 16-OH-E1 Balance	Within range	6.92	ratio	2.85 - 9.88
	2-OH / 4-OH-E1 Balance	Within range	9.91	ratio	6.44 - 12.6
	2-Methoxy / 2-OH Balance	Within range	0.55	ratio	0.4 - 0.7
Androgens and Metabolites (Urine)					
	DHEA-S	Low end of range	217.7	ng/mg	30 - 1500
	Androsterone	High end of range	2644.8	ng/mg	500 - 3000
	Etiocholanolone	Within range	989.2	ng/mg	400 - 1500
	Testosterone	High end of range	113.98	ng/mg	25 - 115
	5a-DHT	Within range	10.7	ng/mg	5 - 25
	5a-Androstanediol	Within range	109.3	ng/mg	30 - 250
	5b-Androstanediol	Within range	126.8	ng/mg	40 - 250
	Epi-Testosterone	Within range	46.1	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.



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:

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

DUTCH Dials

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.

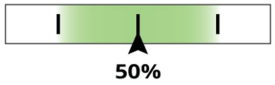
Low Example

Normal Example

High Example

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



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The following video may assist with the interpretation of the Progesterone and Estrogen results: Estrogen tutorial video

This video may assist with the interpretation of the Androgen results: Androgen tutorial video

Androgen Metabolism

- **Androgen Metabolites: DHEA**

DHEA and androstenedione are made almost exclusively by the adrenal gland (although a smaller amount is made in the testes). These hormones appear in urine as DHEA-S (DHEA-Sulfate), androsterone and etiocholanolone.

DHEA peaks for men in their 20's with a slow decline expected with age. DHEA mainly circulates throughout the body as DHEA-s, with interconversion to active DHEA as it reaches various tissues. DHEA is a weak androgen and will predominately convert to androstenedione, which will then convert to testosterone or aromatize to estrone. DHEA-s is made by sulfation, has a much longer half-life than DHEA and lacks a diurnal rhythm, which is why it is considered the best way to assess DHEA levels in the body. DHEA-s levels can be affected both by the

total production as well as by the body’s ability to sulfate DHEA.

The best way to assess the total production of DHEA is to add up these three metabolites. As DHEA production decreases quite significantly with age, we provide the age-dependent ranges.

The DHEA-S is lower than the other major metabolites of DHEA, etiocholanolone and androsterone. DHEA-S is mostly formed in the adrenal glands via sulfation. Inflammation can block sulfation. This lowers the DHEA-S and drives the 5a & 5b-reductase enzymes, metabolizing DHEA away from DHEA-S. Consider addressing inflammation, supporting sulfation with bile acid support (if needed), MSM, sulfur containing foods (such as arugula, asparagus, brassicas, onions, garlic, eggs) and molybdenum. Also consider supporting adrenal health through adaptogens and stress management.

- **Androgen Metabolites: Testosterone**

The DUTCH test measures the total of testosterone glucuronide and testosterone sulfate. These conjugates of testosterone are formed mostly from bioavailable testosterone that undergoes phase 2 metabolism to make it ready for urine excretion.

Testosterone glucuronide is mostly made by the UGT2B17 enzyme, which also makes the glucuronide forms of 5a-DHT and 5b-androstanediol. Genetic variants of this enzyme reduce the urinary levels of these hormones without affecting serum levels. The genetic variants of UGT2B17 vary in the population from 7-80% (variation dependent on genetic ancestry, with the highest rates in those of Asian descent). Heterozygous individuals show milder reductions in urinary testosterone than homozygous. For this reason, low and very low levels of urinary testosterone should be confirmed with serum testing before treatment is applied. Serum testing can include free and total testosterone and SHBG.

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. Testosterone is needed for building bones and muscle mass, regulating body fat distribution and in the production of sperm and red blood cells. Testosterone is also important for libido and downstream production of modest amounts of estrogen.

Age dependent ranges are provided for all androgens as some decline is seen with age. Testosterone levels in healthy men vary widely so it is suggested that these ranges be interpreted with caution and consideration of symptoms. In addition, because estrogen also supports libido, erections and healthy weight management, estrogen levels should be considered along with the testosterone levels when assessing symptoms.

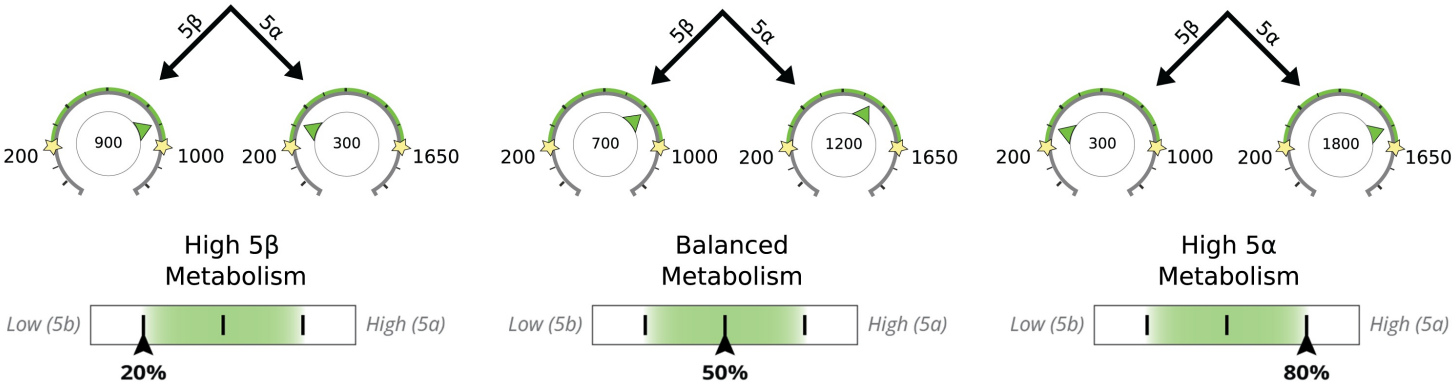
The testosterone result 114ng/mg is above the age dependent range. Review the levels of all androgens, androgenic metabolism, patient's therapies, and symptoms for a complete assessment.

- **Andogen Metabolites: 5a-reductase versus 5b-reductase**

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. However, 5aDHT plays an integral role in supporting bone, muscle and connective tissue integrity and improving brain health through the upregulation of dopamine, which can improve mood and libido.
Metabolites created down the 5b-pathway are significantly less androgenic than their 5a counterparts.

The slider bars below the hormones show the 5a or 5b preference based on the balance between etiocholanolone (5b) and androsterone (5a) as well as 5a-androstanediol and 5b-androstanediol. The slider shows the relative ratio of 5a to 5b products but does not express the absolute value of DHT or if 5a-reductase inhibition is or is not indicated. Consider symptoms and look at the total androgen levels if high androgen symptoms are a concern.

Example of how to read sliders 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 when assessing the validity of urinary testosterone testing in an individual patient. If epi-testosterone is much higher than testosterone, serum testosterone assessment should considered before initiated therapy for low testosterone. Epi-testosterone is suppressed when exogenous testosterone is given, which can serve as a proxy for assessing endogenous testosterone production which can be obscured by the exogenous hormone administration.

Estrogen Metabolism

Over the past few decades research has clarified the importance of healthy estrogen levels and a balanced estrogen to testosterone ratio in men. The testes produce approximately 20% of E2 (Rochira) and the remaining 80% is aromatized from androgens in adipose (fat) tissue, muscle, breast, brain, liver and bone (Rochira). Thus, most of the estrogen in men is aromatized from testosterone, androstenedione, and DHEA in the periphery. The three estrogens (in order of strongest to weakest) are: Estradiol (E2), Estrone (E1) and Estriol (E3). E1 and E2 can interconvert and E3 is a waste product of estradiol and is the weakest of the three estrogens.

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.

To learn more about estrogen metabolism ratios, please read our DUTCH Blog

Progesterone Metabolism

Male progesterone is synthesized in the testes and, to a lesser degree, in the adrenal glands. It's role in men's health is not well understood, although progesterone is known to be involved in sperm activation. In healthy men, progesterone is positively correlated to markers of inflammation.

Metabolites of progesterone are measured in urine, including 5b-pregnanediol and 5a-pregnanediol. 5b-pregnanediol is inactive in the body but is the major metabolite of progesterone. 5a-pregnanediol is often a metabolite of more interest, as it can cross the blood brain barrier and up-regulate GABA activity and is considered neuroprotective to the brain. Both taken together represent the major metabolic end points for progesterone and can be used to represent total progesterone production.

The weighted average of the two progesterone metabolites shows progesterone is in range indicating normal production.

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 2.25.2025)

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 02.25.2025)

	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	1.2	8-OHdG	0	90%	0	8.8
4-OH-E2	0	90%	0	0.25	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	Quinolinate	0	90%	0	12.5
5a-Androstanediol	20%	90%	30	250					
5b-Androstanediol	20%	90%	40	250	**Calculated Values**				
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."

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Female Sample Report
123 A Street
Sometown, CA 90266

Sex Hormones and Metabolites

Last Menstrual Period:

Ordering Provider:
Precision Analytical

DOB: 1982-01-29
Age: 42
Sex: Female

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

Test		Result	Units	Luteal* Range	Postmenopausal Range
Progesterone Metabolites (Urine)					
b-Pregnanediol	Within luteal range	935.7	ng/mg	600 - 2000	60-200
a-Pregnanediol	Low end of luteal range	282.0	ng/mg	200 - 740	15-50
Estrogens and Metabolites (Urine)					
Estrone(E1)	Low end of luteal range	13.67	ng/mg	12 - 26	1.0-7.0
Estradiol(E2)	Within luteal range	2.5	ng/mg	1.8 - 4.5	0.2-0.7
Estriol(E3)	Low end of luteal range	6.5	ng/mg	5 - 18	0.6-4.0
2-OH-E1	High end of luteal range	11.82	ng/mg	5.1 - 13.1	0.3-2.0
4-OH-E1	Within luteal range	1.1	ng/mg	0 - 1.8	0-0.3
16-OH-E1	Below luteal range	0.27	ng/mg	0.7 - 2.6	0.2-0.6
2-Methoxy-E1	Within luteal range	5.66	ng/mg	2.5 - 6.5	0.3-1.4
2-OH-E2	Within luteal range	2.38	ng/mg	0 - 3.1	0-0.52
4-OH-E2	Above luteal range	0.69	ng/mg	0 - 0.52	0-0.12
Total Estrogen	Within range	44.6	ng/mg	35 - 70	3.5-15
Metabolite Ratios					
2-OH / 16-OH-E1 Balance	Above range	43.63	ratio	2.69 - 11.83	
2-OH / 4-OH-E1 Balance	Within range	10.70	ratio	5.4 - 12.62	
2-Methoxy / 2-OH Balance	Within range	0.48	ratio	0.39 - 0.67	
Androgens and Metabolites (Urine)					
DHEA-S	Low end of range	60.0	ng/mg	20 - 750	
Androsterone	Low end of range	440.5	ng/mg	200 - 1650	
Etiocholanolone	Within range	407.0	ng/mg	200 - 1000	
Testosterone	Low end of range	2.73	ng/mg	2.3 - 14	
5a-DHT	Within range	1.6	ng/mg	0 - 6.6	
5a-Androstanediol	Within range	12.1	ng/mg	6 - 30	
5b-Androstanediol	Within range	53.9	ng/mg	12 - 75	
Epi-Testosterone	Within range	5.2	ng/mg	2.3 - 14	

* the Luteal Range is the premenopausal range. When patients are taking oral progesterone this range for progesterone metabolites is not luteal and reflects the higher levels expected when patients take oral progesterone. This test is intended to be taken in the luteal phase of the menstrual cycle (days 19-22 of a 28 day cycle) for premenopausal women. The ranges in the table below may be used when samples are taken during the first few days (follicular) of the cycle, during ovulation (days 11-14) or when patients are on oral progesterone. See the following pages for age-dependent ranges for androgen metabolites.

Additional Normal Ranges	Follicular	Ovulatory	Oral Pg (100mg)
b-Pregnanediol	100-300	100-300	2000-9000
a-Pregnanediol	25-100	25-100	580-3000
Estrone (E1)	4.0-12.0	22-68	N/A
Estradiol (E2)	1.0-2.0	4.0-12.0	N/A

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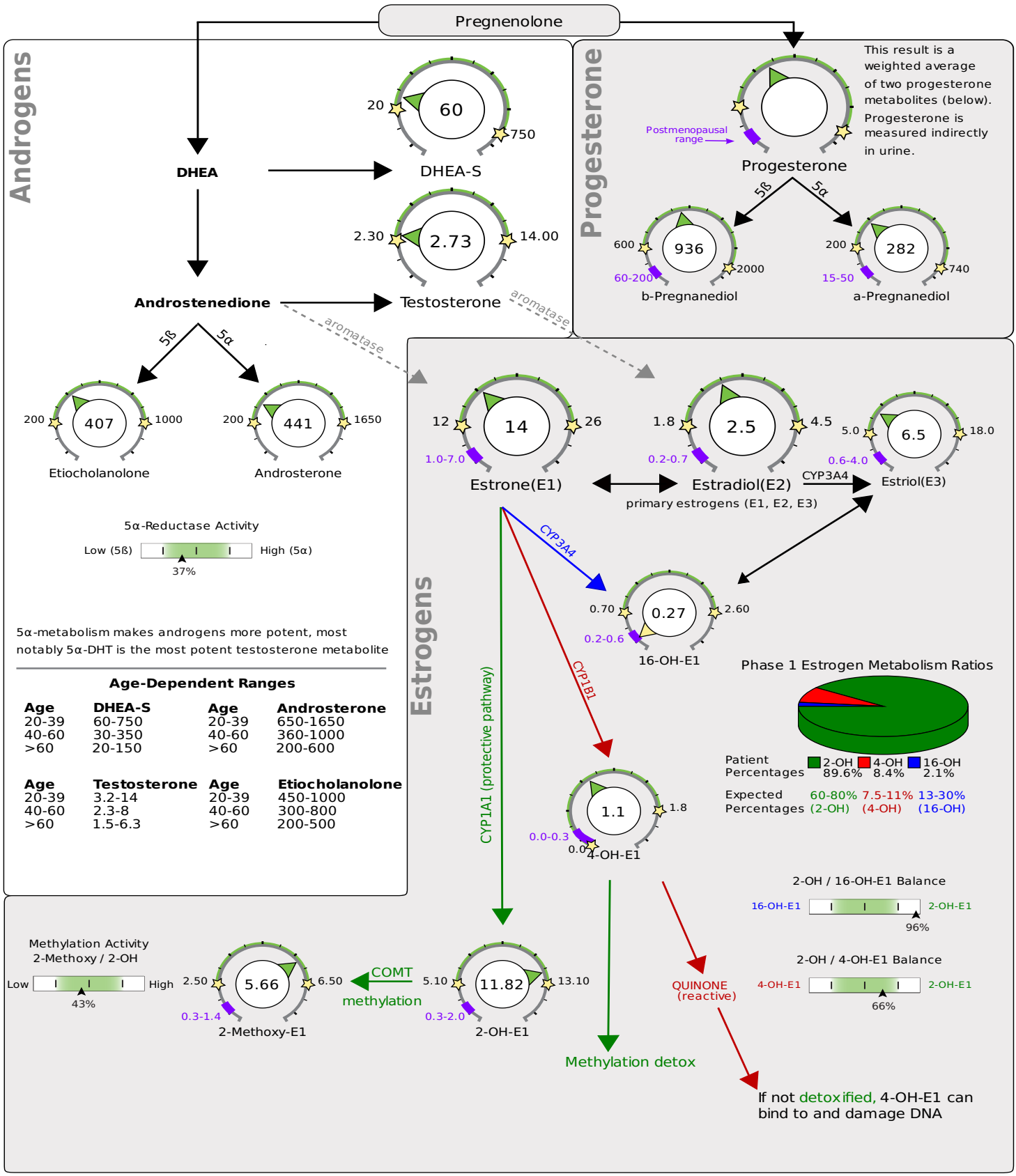

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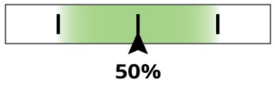

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This video may assist with the interpretation of the Androgen results: Androgen tutorial video

The patient reports regular menstrual cycles.

Progesterone Metabolism

Progesterone is made predominately in the ovaries by the corpus luteum following the release of an egg. Progesterone metabolite levels will increase to the premenopausal luteal range (the range established as the green band between the two gold stars) only after the release of an egg. The level of progesterone metabolites seen on the DUTCH test can help determine if ovulation occurred 5-7 days prior to test collection.

The primary role of progesterone is to prepare the endometrium of the uterus for implantation. In addition, it may balance the effects of estrogen, it is a neurosteroid, it acts as a diuretic and raises basal body temperature.

We are measuring metabolites of progesterone 5b-pregnanediol and 5a-pregnanediol. 5b-pregnanediol has less

activity in the body but does represent a larger percent of total progesterone metabolism overall. 5a-pregnanediol is often a metabolite of more interest, as it can cross the blood brain barrier and up-regulate GABA activity and is considered neuroprotective to the brain. In some women the 5a-pregnanediol is also the cause of PMDD and irritability due to issues with the GABA receptor's inability to adjust for sensitivity to fluctuating neurosteroids (Dr Briden).

If progesterone levels are in the low or lower end of the luteal reference range compared to estrogen levels, women may experience symptoms such as PMS, menorrhagia, mastaglia, moodiness, anxiety, and/or insomnia.

The metabolites of progesterone are excreted in urine (not the progesterone itself). When ordering the DUTCH Complete and DUTCH Plus reports, you will see a Progesterone Serum Equivalent on the summary page 1. The urine metabolites of progesterone have been proven to correlate strongly to serum progesterone. The Progesterone Serum Equivalent is most accurate with values in the luteal range and becomes more approximate at very low numbers in the postmenopausal range. Cycling women with very high progesterone metabolites may also decrease the accuracy of the serum equivalent calculation.
NOTE: If progesterone is taken orally (also with sublingual), these metabolites are elevated from gut metabolism and results do NOT accurately reflect serum levels.

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 ovarian product, estradiol (the strongest estrogen), as well as "total estrogens" may be considered. For women not on HRT, consider the appropriate range (premenopausal or postmenopausal).

- **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. If overall estrogen levels are high, production of 16-OH-E1 may exacerbate high estrogen symptoms. Similarly, a woman with very low levels of estrogens, may have less low estrogen symptoms if 16-OH metabolism is preferred. For example Armamento-Villareal showed that a higher 2-OH-E1/16-OH-E1 ratio correlated to bone loss (a low estrogen symptom). Estriol is thought of as a safer (weaker) estrogen metabolite, but it is important to remember that estriol is actually 16-OH-E2, so generally patients that make a lot of the potentially protective/weak estriol may also make a lot of the estrogenic 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. Similarly, patients with excessive phase I metabolism may have low E1 and E2 levels because of high rates of clearance (as opposed to simply not making a lot of estrogen).
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.

To learn more about estrogen metabolism ratios, please read our DUTCH Blog

Androgen Metabolism

Androgen Metabolites: DHEA

DHEA and androstenedione are made almost exclusively by the adrenal glands. These hormones appear in urine as DHEA-S (DHEA-Sulfate), androsterone and etiocholanolone.
DHEA peaks for men and women in their 20's and 30's, with a slow decline expected with age. DHEA mainly circulates throughout the body as DHEA-s, with interconversion to active DHEA as it reaches various tissues. DHEA is a weak androgen and will predominately convert to androstenedione, which will then convert to testosterone or estrogen. DHEA-s is made by sulfation, has a much longer half-life than DHEA and largely lacks a diurnal rhythm, which is why it is considered the best way to assess DHEA levels in the body. DHEA-s levels can be affected both by the total production as well as by the body's ability to sulfate DHEA.
The best way to assess the total production of DHEA is to add up these three metabolites. As DHEA production decreases quite significantly with age, we provide the age-dependent ranges. Adrenals serve as the main source of estrogen, progesterone and testosterone for post-menopausal women.

- **Androgen Metabolites: Testosterone**

The DUTCH test measures the total of testosterone glucuronide and testosterone sulfate. These conjugates of testosterone are formed mostly from bioavailable testosterone that undergoes phase 2 metabolism to make it ready for urine excretion. Females make most of their DHEA in the adrenal gland and a fraction of that DHEA trickles down metabolically to testosterone. Testosterone is also made by the ovaries.

Testosterone glucuronide is mostly made by the UGT2B17 enzyme, which also makes the glucuronide forms of 5a-DHT and 5b-androstanediol. Genetic variants of this enzyme reduce the urinary levels of these hormones without affecting serum levels. The genetic variants of UGT2B17 vary in the population from 7-80% (variation dependent on genetic ancestry, with the highest rates in those of Asian descent). Heterozygous individuals show milder reductions in urinary testosterone than homozygous. For this reason, low and very low levels of urinary testosterone should be confirmed with serum testing before treatment is applied. Serum testing can include free and total testosterone and SHBG.

Testosterone levels may be better understood by also considering its downstream metabolites (5a-androstanediol, 5bandrostanediol). Technically, these metabolites can also be formed from DHEA metabolites without going through the testosterone pathway, but they generally tend to correlate with testosterone production.

Testosterone levels normally decline with age. Age dependent ranges are provided. Perimenopausal testosterone levels can transiently increase before declining again.

Epi-testosterone (epi-T) is made at about the same rate as testosterone but is not androgenic. In cases where testosterone in urine is low, such as with the UGT2B17 deletion discussed above, epi-T may be used as a proxy for testosterone production, meaning that higher epi-T levels may indicate that a low testosterone result is falsely low. After menopause, epi-T production is less reliable as a marker of testosterone production as epi-T levels drop more sharply than does testosterone during the menopause transition. While epi-T may have limited utility in some cases, it does enhance the picture when taking androgen metabolites together as a whole. Androgens, specifically DHT and testosterone, help to support skin, connective tissue, bone and muscle integrity and promote dopamine conversion in the brain, which can help with mood and libido.

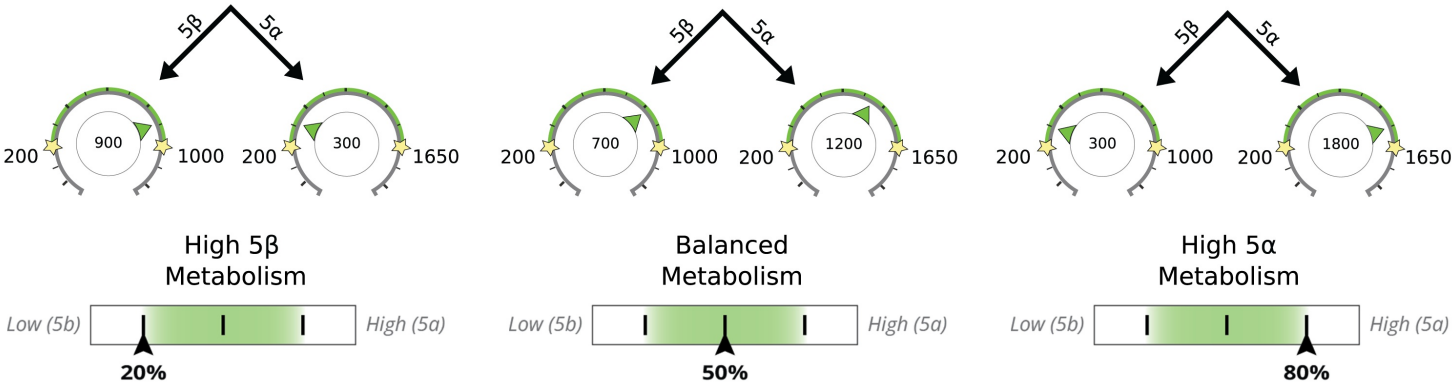
The testosterone result 2.73ng/mg is in range for the patient's age. Review the levels of all androgens, androgenic metabolism, and patient symptoms for a complete assessment.

- **Androgen Metabolites: 5a-reductase versus 5b reductase**

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, including scalp hair loss, hirsutism, acne and oily skin.
Metabolites created down the 5b-pathway are significantly less androgenic than their 5a counterparts.

The slider bars below the hormones show the 5a or 5b preference based on etiocholanolone (5b) and androsterone (5a) results. The slider shows the relative ratio of 5a to 5b products but does not express the absolute value of DHT or if 5a-reductase inhibition is or is not indicated. Consider symptoms and look at the 5a-DHT result if high androgen symptoms are a concern. Progesterone metabolites are also metabolized by 5a and 5b enzymes and the balance between its two metabolites can be useful to confirm a 5a or 5b preference overall (or tissue specific preference).

Example of how to read sliders for 5a-reductase activity:



When assessing androgens in women, it is important to consider DHEA and testosterone production, 5a-metabolism patterns as well as the patient symptoms. For example, a woman with higher levels of DHEA and testosterone will often have high androgen symptoms (facial hair, thinning scalp hair, etc.) exacerbated by 5a-metabolism.

If, on the other hand, she prefers 5b-metabolism she may not express high androgen symptoms in spite of higher levels of testosterone because 5b is the less androgenic pathway.

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 when assessing the validity of urinary testosterone testing in an individual patient. If epi-testosterone is much higher than testosterone, serum testosterone assessment should considered before initiated therapy for low testosterone. Epi-testosterone is suppressed when exogenous testosterone is given, which can serve as a proxy for assessing endogenous testosterone production which can be obscured by the exogenous hormone administration.

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 2.25.2025)

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 02.25.2025)

	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	3.1	8-OHdG	0	90%	0	5.2
4-OH-E2	0	80%	0	0.52	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	Quinolinate	0	90%	0	9.6
5a-Androstanediol	20%	80%	6	30					
5b-Androstanediol	20%	80%	12	75	**Calculated Values**				
Epi-Testosterone	20%	80%	2.3	14	Total DHEA Production	20%	80%	500	3000
a-THF	20%	90%	75	370	Total Estrogens	20%	80%	35	70
b-THF	20%	90%	1050	2500	Metabolized Cortisol	20%	90%	2750	6500
b-THE	20%	90%	1550	3800	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."