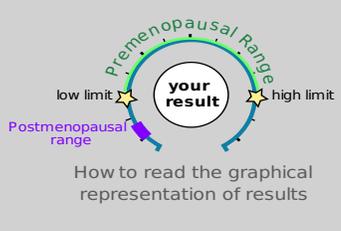


**Ordering physician:**  
Precision Analytical

**DOB:**1976-01-01  
**Gender:** Female

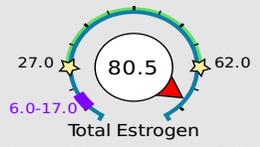
**Collection Times:**  
2015-08-16 05:00PM  
2015-08-16 10:00PM  
2015-08-17 06:00AM  
2015-08-17 08:00AM

**Hormone Testing Summary**

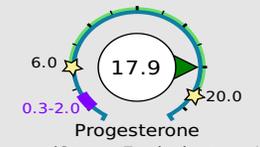


How to read the graphical representation of results

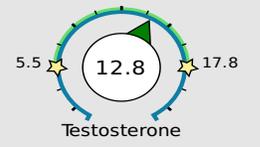
**Sex Hormones**



**Total Estrogen**  
(Sum of 8 Estrogen Metabolites)



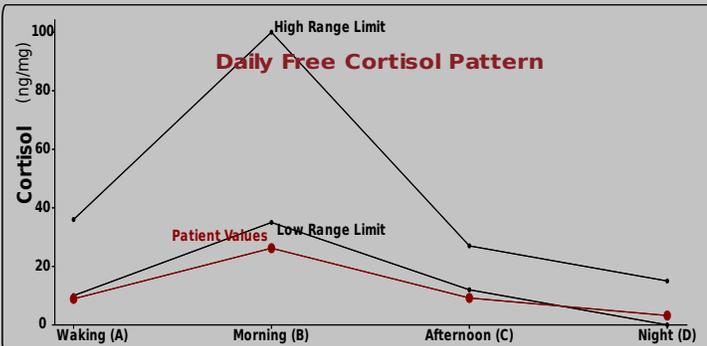
**Progesterone**  
(Serum Equivalent, ng/mL)



**Testosterone**

See Pages 2 & 3 for a thorough breakdown of sex hormone metabolites

**Adrenal Hormones**



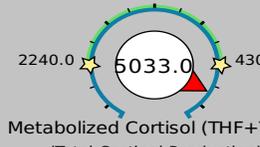
Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production. See pages 4 and 5 for a more complete breakdown.

**Total DHEA Production**

Age	Range
20-40	800-2500
40-60	530-1550
>60	400-1350



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



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

cortisol metabolism

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
Progesterone	Suprene	5	100 mg/ml	7/6/15	1	11 mos.

All units are given in ng/mg creatinine

Patient reports regular menstrual cycles

Last Menstrual Period - 2015-07-27

Not taking any listed hormones

Do you take DIM/1-3-C regularly?  Yes  No

List Any other relevant drugs, supplements or others:  
Magnesium Glycinate (Leta) 600mg  
Adrenal Support 2

Progesterone Serum Equivalent is a calculated value based on urine pregnanediol. This value may not accurately reflect serum when progesterone is taken by mouth.



**Accession # 00212403**

Sample Female Report  
123 A Street  
Sometown, CA 90266



**Sex Hormones and Metabolites**

**Ordering physician:**  
Precision Analytical

**DOB:**1976-01-01  
**Gender:** Female

**Collection Times:**  
2015-08-16 05:00PM  
2015-08-16 10:00PM  
2015-08-17 06:00AM  
2015-08-17 08:00AM

Category	Test	Result	Units	Normal Range
<b>Progesterone Metabolism</b>				
	b-Pregnanediol	Within range	996.0	ng/mg 450 - 1400
	a-Pregnanediol	High end of range	499.0	ng/mg 120 - 500
<b>Androgen Metabolism</b>				
	DHEAS	Above range	428.0	ng/mg 23 - 350
	Androsterone	Above range	1400.0	ng/mg 399 - 1364
	Etiocholanolone	Low end of range	390.0	ng/mg 371 - 765
	Testosterone	Within range	12.8	ng/mg 5.5 - 17.8
	5a-DHT	Within range	2.1	ng/mg 0 - 8.8
	5a-Androstanediol	Within range	53.1	ng/mg 22 - 66
	5b-Androstanediol	Within range	12.1	ng/mg 6 - 32
	Epi-Testosterone	Within range	14.1	ng/mg 4.5 - 22.3
<b>Estrogen Metabolites</b>				
	Estrone(E1)	Above range	42.5	ng/mg 12 - 26
	Estradiol(E2)	Above range	7.4	ng/mg 1.8 - 4.5
	Estriol(E3)	Above range	22.5	ng/mg 5 - 18
	2-OH-E1	Below range	3.7	ng/mg 4.6 - 14.4
	4-OH-E1	Within range	1.1	ng/mg 0 - 1.8
	16-OH-E1	Within range	2.9	ng/mg 1 - 3.5
	2-Methoxy-E1	Below range	1.2	ng/mg 2 - 5.5
	2-OH-E2	Within range	0.4	ng/mg 0 - 1.2

Normal Ranges	Luteal	Postmenopausal	Follicular	Ovulatory
Estrone (E1)	14-27.1	1.3-6.7	4.0-12.0	22-68
Estradiol (E2)	2.0-4.9	0.2-0.8	1.0-2.0	4.0-12.0
Estriol (E3)	5.6-23	0.8-3.7	N/A	N/A
2-OH-E1	4.6-14.4	0.4-1.9	N/A	N/A
4-OH-E1	0-1.8	0-0.3	N/A	N/A
16-OH-E1	1.3-4.6	0.1-0.6	N/A	N/A
2-Methoxy-E1	2.9-5.9	0.2-1.0	N/A	N/A
<b>Oral Pg (100mg)</b>				
a-Pregnanediol	80-750	5.0-34	750-2300	25-100 25-100
b-Pregnanediol	400-2300	28-135	2300-6000	100-300 100-300

**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.



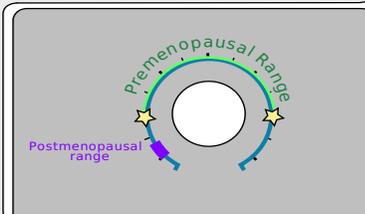
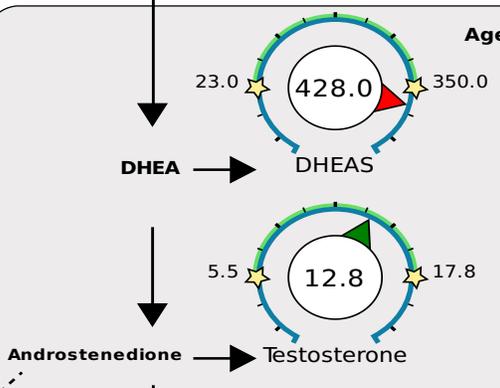
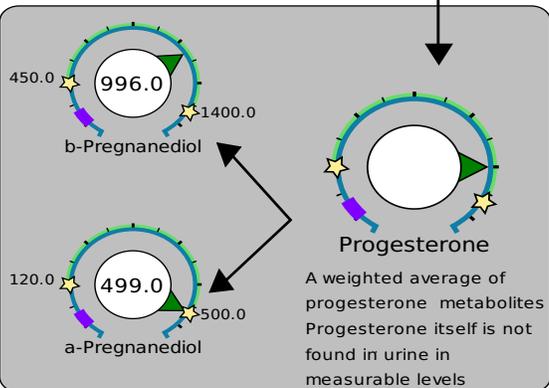
**Progesterone Metabolism female**

Pregnenolone

**Androgen Metabolism**

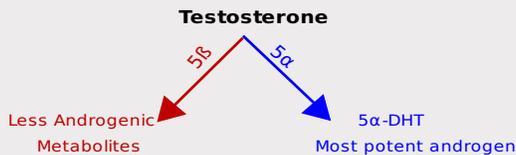
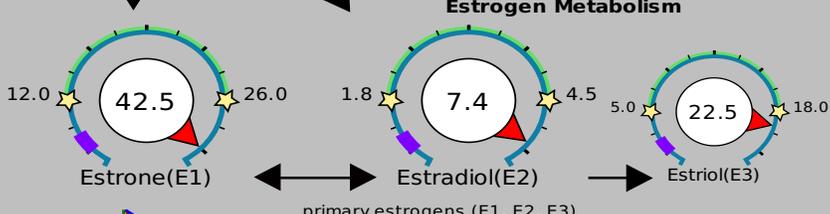
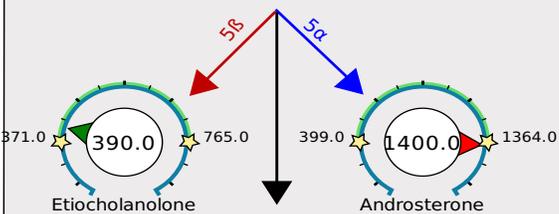
**Age-Dependent DHEAS Ranges**

Age	DHEAS
20-40	30-350
40-60	10-100
>60	5-50

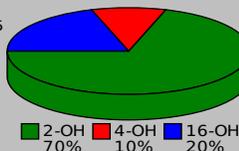


**Androstenedione**

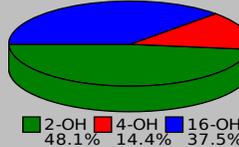
**Estrogen Metabolism**



**Normal Estrogen Metabolism**

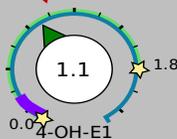


**Patient Estrogen Metabolism**

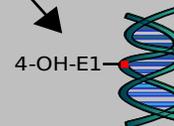


5α-metabolism makes androgens more androgenic, most notably 5α-DHT is the most potent testosterone metabolite (~3x more potent than testosterone itself). 5α-Reductase activity is assessed using the ratio of Androsterone (5α) to Etiocholanolone (5β).

protective pathway



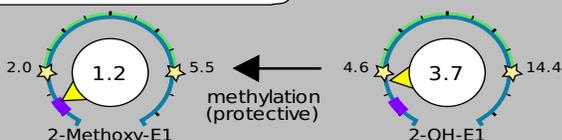
4-Methoxy-E1 (Protective, but not enough in urine to measure)



If not methylated, 4-OH-E1 can bind to and damage DNA



Methylation-activity  
2-Methoxy/2-OH





**Accession # 00212403**  
 Sample Female Report  
 123 A Street  
 Sometown, CA 90266



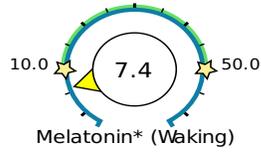
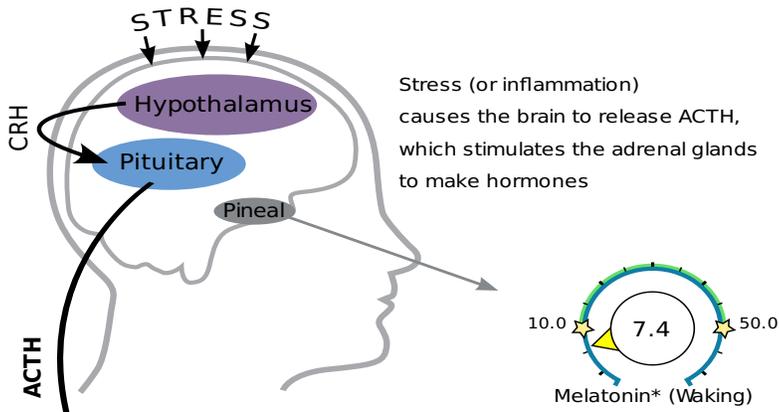
**Advanced Adrenal Assessment**

**Ordering physician:**  
 Precision Analytical

**DOB:**1976-01-01  
**Gender:** Female

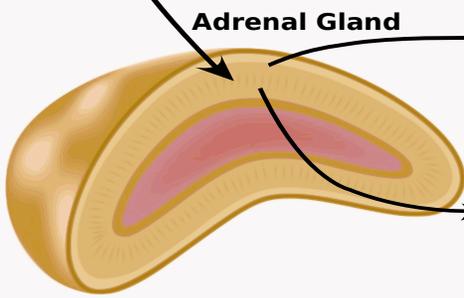
**Collection Times:**  
 2015-08-16 05:00PM  
 2015-08-16 10:00PM  
 2015-08-17 06:00AM  
 2015-08-17 08:00AM

Category	Test		Result	Units	Normal Range
<b>Creatinine</b>					
	Creatinine A (Waking)	Within range	0.96	mg/ml	0.3 - 3
	Creatinine B (Morning)	Within range	1.71	mg/ml	0.3 - 3
	Creatinine C (Afternoon)	Within range	0.55	mg/ml	0.3 - 3
	Creatinine D (Night)	Within range	0.99	mg/ml	0.3 - 3
<b>Daily Free Cortisol and Cortisone</b>					
	Cortisol A (Waking)	Below range	8.9	ng/mg	10 - 36
	Cortisol B (Morning)	Below range	26.2	ng/mg	35 - 100
	Cortisol C (Afternoon)	Below range	9.2	ng/mg	12 - 27
	Cortisol D (Night)	Within range	3.2	ng/mg	0 - 15
	Cortisone A (Waking)	Low end of range	34.0	ng/mg	30 - 90
	Cortisone B (Morning)	Within range	108.0	ng/mg	80 - 185
	Cortisone C (Afternoon)	Low end of range	46.0	ng/mg	40 - 85
	Cortisone D (Night)	Within range	30.0	ng/mg	0 - 40
	24hr Free Cortisol	Below range	48.0	ug	80 - 180
	24hr Free Cortisone	Low end of range	218.0	ug	210 - 370
<b>Cortisol Metabolites and DHEAS</b>					
	a-Tetrahydrocortisol (a-THF)	Above range	600.0	ng/mg	90 - 320
	b-Tetrahydrocortisol (b-THF)	High end of range	1310.0	ng/mg	750 - 1450
	b-Tetrahydrocortisone (b-THE)	Above range	3123.0	ng/mg	1300 - 2560
	Metabolized Cortisol (THF+THE)	Above range	5033.0	ng/mg	2240 - 4300
	DHEAS	Above range	428.0	ng/mg	23 - 350
<b>Melatonin (*measured as 6-OH-Melatonin-Sulfate)</b>					
	Melatonin* (Waking)	Below range	7.4	ng/mg	10 - 50



**Total DHEA Production**

Age	Range
20-40	800-2500
40-60	530-1550
>60	400-1350



**DHEA**

A patient's catabolic vs anabolic balance can be estimated by observing relative DHEA (anabolic) vs cortisol (catabolic) production



Total DHEA Production (DHEAS + Etiocholanolone + Androsterone)

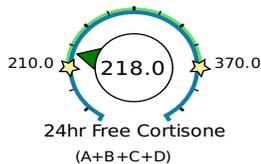
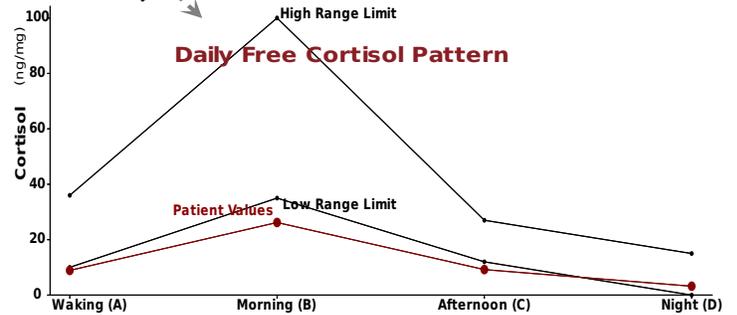
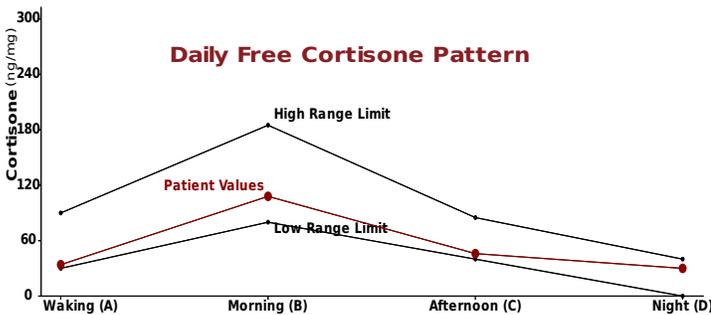
**Cortisol**

**Cortisol Metabolism**

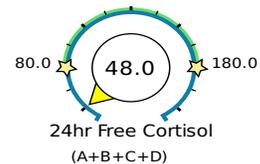
**Circulating Free Cortisol**



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



Cortisol and Cortisone interconvert (11b-HSD) and are metabolized to THF & THE for excretion



More cortisone metabolites (THE)

More cortisol metabolites (THF)

# Patient Notes

**NOTE: The report format has changed recently with the addition of a summary page when ordering the dutch Complete. New features include Total Estrogen (a total of all measured estrogens), Progesterone Serum Equivalent (based on excellent urine, serum correlation) and Total DHEA Production (total of DHEA metabolites).**

Thank you for testing with Precision Analytical, Inc. Due to the complexity of the analysis, you may need the guidance of your healthcare provider in order to properly interpret some of your results. The information here is intended to assist you in understanding your results in conjunction with your visit with your provider and is not intended to diagnose or treat any specific disease. You may want to skip to "Reading the Report" first for an explanation of how to read the report and background information on urine hormone testing before continuing with the report. You will find information in the comments for each subsection of each testing profile. Comments in the report that are specific to you ARE IN ALL CAPS. The other information is general information that we hope you will find useful in understanding your results. Please refer questions to your healthcare provider.

The following video link(s) may help patients understand their dutch results. If you have only a hardcopy of the results, the video names can be easily found in our video library at [www.PrecisionHormones.com](http://www.PrecisionHormones.com). Any clinical conclusions from results should be made exclusively by your provider. These results and videos are NOT intended to diagnose or treat specific disease states.

The following videos may assist with the interpretation of your Progesterone results:  
Postmenopausal Women - [Progesterone-post-01](#)

Premenopausal Women - [Progesterone-pre-02](#)

The following videos may assist with the interpretation of your Estrogen results:  
Postmenopausal Women - [Estrogen-post-01](#)

Premenopausal Women - [Estrogen-pre-high-04](#)

This video may assist with the interpretation of your Androgen results: [Androgens-01](#)

YOU REPORTED SIGNIFICANT SYMPTOMS RELATED TO ESTROGEN DEFICIENCY.

**Progesterone Metabolism:** The primary role of progesterone is to balance the strong effects of estrogen. Progesterone metabolites are measured and reflect progesterone levels well. If levels are in the lower part of the reference range compared to estrogen levels, symptoms of too much estrogen may occur.

When ordering the DUTCH Complete, you will see Progesterone Serum Equivalent on the summary page. The urine metabolites of progesterone have been proven to correlate strongly enough to serum progesterone to provide this value. The correlation is the strongest for values within the premenopausal luteal range. Urine metabolites can at times result in somewhat higher serum equivalent results in the postmenopausal range. For this reason the postmenopausal Serum Equivalent range is slightly higher than typical serum ranges. NOTE: If progesterone is taken orally (also with sublingual), these metabolites are elevated from gut metabolism and results do NOT accurately reflect serum levels.

**YOU REPORTED THE USE OF VAGINAL PROGESTERONE. SERUM LEVELS INCREASE TO HEALTHY LEVELS WITH APPROPRIATE DOSES OF VAGINAL PROGESTERONE. URINE METABOLITES SHOULD LIKEWISE INCREASE TO PREMENOPAUSAL LEVELS.**

**Androgen Metabolism:** This group of hormones is typically thought of as "male" hormones, but they play a key role for women as well. The ovaries and adrenal glands make androgens. Testosterone contributes 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). Testosterone deficiency can lead to decreased sexual function, vaginal dryness, and bone loss.

**5a-Reductase Activity:** Many hormones are metabolized by the 5a or the 5b pathways. The "fan" style gauge at the bottom of this section gives you an idea of which pathway your body favors. Why does this matter? The 5a pathway makes the very potent (3x more than testosterone) 5a-DHT from testosterone. If the your body heavily favors the 5a pathway, this may be accompanied by clinical signs of high androgens such as excess facial hair growth, scalp hair loss, acne, irritability and oily skin. For men, too much 5a-DHT is not desirable for prostate cancer risk. 5b metabolites are much less potent, and do not exert the same effects as 5a-DHT.

**Estrogen Metabolism:** Estradiol (E2) is the most potent estrogen and you should evaluate it along with estrone (E1) and estriol (E3) to check your overall estrogen status. E1 and E2 are cleared from the body through three pathways. As you can see from the pie chart, usually the 2-OH pathway is the main pathway and these "good" estrogens are protective against estrogen-related cancers. 16-OHE1 is sometimes called a "bad" estrogen and 4-OHE1 is even worse (carcinogenic). If you are making less of the good estrogens or more of the bad ones compared to "Normal Estrogen Metabolism," this can be improved by eating cruciferous vegetables or with certain supplements (such as DIM).

The last step of estrogen metabolism is methylation. The Methylation Index shows how well the body is achieving this important step where 2-Methoxy-E1 is made. Methylation helps protect the body against the harmful effects of 4-OH estrogens.

PATIENTS TYPICALLY METABOLIZE A MUCH HIGHER PERCENTAGE OF THEIR ESTROGENS DOWN THE MORE PROTECTIVE 2-OH PATHWAY. SOME CONSIDER THESE (2-OH) METABOLITES TO BE MORE BENEFICIAL, AND YOU MAY WANT TO CONSIDER PRODUCTS LIKE DIINDOLYLMETHANE (DIM) OR INDOLE-3-CARBINOL THAT PROMOTE THIS PATHWAY. THIS TYPICALLY LOWERS MOST OF THE OTHER ESTROGENS, INCLUDING E1 AND E2, SO IT IS SOMETHING TO BE CONSIDERED CAREFULLY WITH YOUR PROVIDER. IF PATIENTS ARE TAKING OR CONSIDERING HORMONE REPLACEMENT THERAPY, THESE PRODUCTS MAY BE CONSIDERED BUT A HIGHER DOSE OF ESTROGEN MAY BE NEEDED FOR THE SAME CLINICAL EFFECT IF CONCURRENTLY TAKEN.

**ADVANCED ADRENAL ASSESSMENT:** When you are under stress (physical or psychological), your HPA-axis (brain talking to adrenal glands) is prompted to produce ACTH which stimulates the adrenal gland to make the stress hormone cortisol and to a lesser extent DHEA-S. Most cortisol is then metabolized to "metabolized cortisol" and levels of both "free" and "metabolized" cortisol 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 right after going to sleep. Cortisone is the inactive form of cortisol. Its pattern is of secondary importance, but at times can give additional clarity to your provider.

The daily total of free cortisol is approximated by adding up the four individual measurements of free cortisol. This represents circulating cortisol. Metabolized cortisol is actually a better marker when looking at total cortisol production.

WHILE FREE CORTISOL LEVELS ARE LOW, THESE RESULTS CAN BE SOMEWHAT MISLEADING IN THIS CASE. OVERALL CORTISOL PRODUCTION IS BEST APPROXIMATED BY LEVELS OF METABOLIZED CORTISOL, WHICH ARE ELEVATED. THIS IMPLIES THAT OVERALL ADRENAL ACTIVITY IS ELEVATED.

**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). 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. In some cases this index is important for overall understanding of why symptoms of high or low cortisol may be predominating. In other cases this index is not critically important.

THE RATIO BETWEEN YOUR THF/THE SHOWS A PREFERENCE FOR CORTISONE. THIS CONVERSION INTO CORTISONE IS CONTRIBUTING TO YOUR DEFICIENT CORTISOL LEVELS, WHICH YOU MAY WANT TO ADDRESS WITH YOUR HEALTHCARE PROVIDER.

**Reading the Report:** The first page of the lab report is a classic lab report showing each result and the respective range of each hormone. Reference ranges shown are those of young healthy females collecting on days 19-21 (mid-luteal phase) of the menstrual cycle. 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 your result (represented by the "needle" of the gauge) and the area between the stars represents the reference range.

The "fan" style gauges are used for indexes/ratios. These usually tell you how "turned up" a particular metabolic process is. Because these values are all based on ratios there are no values or units, but they give a general idea of a particular relationship. The middle of the gauge represents an average value, while the lines towards the edge represent results lower or higher than what is usually expected.

**UPDATE: The DUTCH Complete report now also has a summary page for a quick overview of the most vital information. This includes a screenshot of the reported therapies.**

General Overview: Hormones are known as "chemical messengers." They are formed in one part of the body, sent throughout the rest, and do their work anywhere their respective receptor is present. In men, for example, testosterone is produced primarily in the testes and then sent throughout the body. The skin in certain areas has a lot of receptors for testosterone (androgen receptors) that interact with the hormone to generate the hormonal effect of increasing facial and body hair, for example.

Typically parent hormones such as estradiol (primary estrogen), progesterone, DHEA, and cortisol (stress hormone) are made by organs designed specifically for their production. These hormones are then sent throughout the body to exert their influence and are also metabolized. These metabolites can also exert significant influence. Estradiol, as an example, can be turned into 2-OH and 4-OH estradiol. One of these is protective and one is carcinogenic, so measuring parent hormones and their metabolites is very important when evaluating a person's overall hormonal picture. There are many different types of hormones, but all of those measured in this test are considered "steroid hormones."

Cholesterol is the backbone to all steroid hormones, and it sits at the top of the hormone cascade. The adrenal glands, as an example, take in cholesterol make the hormone pregnenolone, which is then converted in the adrenal into both cortisol and DHEA-S. Estradiol (the primary estrogen) and progesterone are slightly more complicated but also start with cholesterol when made by the ovaries of cycling women. Each of these hormones can also be produced in other places in the body from the hormone preceding it in the cascade. Estrogens can be made to some extent from DHEA, for example, but at much lower rates as compared to ovarian production (for premenopausal women).

Before hormones can be found in the urine, they must be water-soluble (since urine is mostly water) or they won't be excreted in large amounts. Most of the steroid hormones are not water-soluble. The liver or kidney must first attach another molecule (in most cases similar to a sugar molecule) to a hormone through a process known as 'conjugation' in order for it to be properly excreted in the urine.

This process of making the hormones more easily excreted is called phase II detoxification. As an example, conjugated testosterone that has gone through phase II detoxification is found in the urine 100 times more than actual free (non-conjugated) testosterone. In the lab, we convert these conjugated hormones back into their original form (testosterone, in this case) and then measure them. For the most part, these measurements reflect the bioavailable (or active) amount of hormone in the body.

Cortisol and cortisone are much more water soluble and therefore are better measured as 'free' hormones (conjugates are ignored). A significant amount of scientific research has been done over the years to validate the usefulness of measuring 'free' cortisol and cortisone as well as the conjugated forms of the other hormones in urine. Epi-testosterone is considered "for research only" as there is no appropriate proficiency testing for this compound currently.

# Provider Notes

**NOTE: The report format has changed recently with the addition of a summary page when ordering the dutch Complete. New features include Total Estrogen (a total of all measured estrogens), Progesterone Serum Equivalent (based on excellent urine, serum correlation) and Total DHEA Production (total of DHEA metabolites).** If this is your first report, you are encouraged to skip to the last two paragraphs first for an explanation of how to read the report and background information on urine hormone testing. The patient comments may serve as introductory level. Provider comments discuss more complex aspects of the test. Comments in the report that are specific to your patient ARE IN ALL CAPS. The other information is general information that we hope you will find useful in understanding your patient's results. Reference ranges updated 7/23/2015.

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Premenopausal Women - [Progesterone-pre-02](#)

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Premenopausal Women - [Estrogen-pre-high-04](#)

This video may assist with the interpretation of your Androgen results: [Androgens-01](#)

THE PATIENT REPORTS SIGNIFICANT SYMPTOMS OF ESTROGEN DEFICIENCY.

**Progesterone Metabolism:** Very little progesterone is found in urine, so b-Pregnanediol is typically used a surrogate marker because it is the most abundant metabolite, but we also test the corresponding a-pregnanediol. The average of the two metabolites is reported for progesterone. When the relative levels of estrogen are higher than those for progesterone symptoms of estrogen dominance may occur.

When ordering the DUTCH Complete, you will see Progesterone Serum Equivalent on the summary page. The urine metabolites of progesterone have been proven to correlate strongly enough to serum progesterone to provide this value. The correlation is the strongest for values within the premenopausal luteal range. Urine metabolites can at times result in somewhat higher serum equivalent results in the postmenopausal range. For this reason the postmenopausal Serum Equivalent range is slightly higher than typical serum ranges. NOTE: If progesterone is taken orally (also with sublingual), these metabolites are elevated from gut metabolism and results do NOT accurately reflect serum levels.

**THE PATIENT REPORTS USE OF VAGINAL PROGESTERONE. SERUM LEVELS INCREASE TO LUTEAL LEVELS WITH APPROPRIATE DOSES OF VAGINAL PROGESTERONE. URINE METABOLITES SHOULD LIKEWISE INCREASE TO PREMENOPAUSAL LEVELS.** This [video](#) may assist with understanding results in this situation.

**Androgen Metabolism:** Testosterone is made in the ovaries as well as the adrenal glands. In postmenopausal women adrenal production is the primary source of testosterone. 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 excreted. As such, a-androstenediol may best represent a-DHT even though its metabolic precursor is more biologically active and well known. 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.

**5a-Reductase Activity:** The competing enzymes 5a and 5b-reductase act on the androgens androstenedione (creating androsterone and etiocholanolone) and testosterone (creating a-DHT and b-DHT). They also metabolize progesterone, and cortisol (a/b-THF). 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). 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:** There are two primary issues with respect to estrogens. 1) Estrogen production (is the patient deficient, sufficient, or in excess?) and 2) Estrogen metabolism (is the metabolism of estrogen favorable or unfavorable with respect to hydroxylation and methylation pathways?)

While estradiol (E2) is the most potent estrogen, levels of estrone (E1) and estriol (E3) should also be considered when evaluating the patient's estrogen production. You want to compare the patient's distribution of metabolites from the pie chart to "Normal Estrogen Metabolism." If they are making considerably less of the protective 2-OH estrogens, you may want to consider something to up-regulate this metabolism (DIM, I-3-C, etc). Be advised increasing 2-OH metabolism will likely lower E1 and E2. 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 female reference range for the ratio with our methodology is 2.4-6.0.

The methylation index will show you how effectively the patient is turning 2 and 4-OH estrogens into methoxy estrogens. Methylation protects against potentially harmful 4-OH estrogens. Supporting the methylation pathway should be considered if this index is low.

PATIENTS TYPICALLY METABOLIZE A MUCH HIGHER PERCENTAGE OF THEIR ESTROGENS DOWN THE MORE PROTECTIVE 2-OH PATHWAY. DIINDOLYLMETHANE (DIM) OR INDOLE-3-CARBINOL CONTAINING PRODUCTS CAN HELP MOVE ESTROGENS MORE EFFICIENTLY DOWN THIS PATHWAY. THIS TYPICALLY LOWERS MOST OF THE OTHER ESTROGENS, INCLUDING E1 AND E2. IF PATIENTS ARE TAKING OR CONSIDERING HORMONE REPLACEMENT THERAPY, THESE PRODUCTS MAY BE CONSIDERED BUT A HIGHER DOSE OF ESTROGEN MAY BE NEEDED FOR THE SAME CLINICAL EFFECT IF CONCURRENTLY TAKEN.

**ADVANCED ADRENAL ASSESSMENT:** 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 the ACTH, a hormone. ACTH stimulates the adrenal glands to make 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.

**Diurnal Free Cortisol Pattern:** The primary reason for the timing of urine collections for this test is to assess the diurnal pattern of cortisol (and to a lesser extent cortisone). 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 expected pattern. Dysfunctional diurnal patterns have been associated with health-related problems such as fatigue. While the diurnal pattern of cortisol is of primary interest, the cortisone pattern may provide additional clarity in certain situations. Cortisol levels usually are at their lowest around 1am and peak in the first 30-60 minutes following waking. The waking sample represents the total of free cortisol throughout the sleeping period.

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.

WHILE FREE CORTISOL LEVELS ARE LOW, THESE RESULTS CAN BE SOMEWHAT MISLEADING IN THIS CASE. OVERALL CORTISOL PRODUCTION IS BEST APPROXIMATED BY LEVELS OF METABOLIZED CORTISOL, WHICH ARE ELEVATED. THIS IMPLIES THAT OVERALL HPA-AXIS ACTIVITY IS ELEVATED. CORTISOL CLEARANCE IS UP-REGULATED IN THIS PATIENT, LEAVING THEM WITH LOW LEVELS OF FREE CORTISOL. THE PATIENT'S CORTISOL STATUS MAY BE DIFFERENT DEPENDING ON LOCATION WITHIN THE BODY. FOR EXAMPLE, THE CONVERSION FROM NORADRENALINE TO ADRENALINE IS DRIVEN BY CORTISOL AND TAKES PLACE WITHIN THE ADRENAL MEDULLA. IN THIS CASE, THIS AREA IS LIKELY FLOODED WITH HIGH LEVELS OF CORTISOL FORCING CONVERSION TO ADRENALINE, WHEREAS THE BRAIN (WHERE CORTISOL HAS NEGATIVE FEEDBACK ON ACTH PRODUCTION) MAY BE CORTISOL DEFICIENT. EFFORTS TO INCREASE HPA-AXIS ACTIVITY MAY EXACERBATE SOME SYMPTOMS. CALMING THE HPA-AXIS, WHILE SUPPORTING IT IN WAYS THAT ARE NOT EXCITATORY, MAY BE THE BEST COURSE OF ACTION.

**Cortisol-Cortisone Balance:** The back-and-forth conversion of cortisol and its inactive form, cortisone is not a tug-of-war going on between the two 11b-HSD enzyme types within a particular tissue. These two actions (activation to cortisol and deactivation to cortisone) happen in different compartments within the body. The deactivation of cortisol to cortisone (11b-HSD II) occurs predominantly in the kidneys, colon, and saliva glands. The local formation of cortisone from cortisol in the kidney is strongly reflected in urine. This makes the ratio of free cortisone and cortisol a good index of this local renal deactivation (11b-HSD II) but the free cortisol-cortisone ratio does not speak to the overall predominance of cortisol or cortisone. 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), and it is the balance between these metabolites that best reflects the overall predominance of cortisol or cortisone. The gauge at the bottom of the adrenal graphical page reflects the ratio (aTHF+bTHF)/THE. 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.

THE PATIENT'S THF/THE AND CORTISOL TO CORTISONE RATIOS IMPLY A PREFERENCE FOR CORTISONE (RELATIVE TO CORTISOL). THIS IS LIKELY A CONTRIBUTING FACTOR TO THE SOMEWHAT DEFICIENT CORTISOL LEVELS ALTHOUGH THE PATIENT DOES NOT REPORT SIGNIFICANT FATIGUE. IF ADRENAL SUPPORT IS CONSIDERED, THE INCLUSION OF LICORICE ROOT WILL ASSIST IN BLOCKING THE DEACTIVATION OF CORTISOL TO CORTISONE AS WELL AS THE METABOLISM OF CORTISOL BY 5b-REDUCTASE.

**Reading the Report:** The first page of the lab report is a classic lab report showing each result and the respective range of each hormone. Reference ranges shown are those of young healthy individuals with females collecting on days 19-21 (mid-luteal phase) of the menstrual cycle. 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. Each gauge is plotted so that an identical place on two gauges represents the same result relative to the normal range. For example, a result directly in the middle of the gauge represents an average person's result, not the mathematical average of the high and low limits of the range. This makes it easy to spot abnormally low or high metabolism at different points in the hormone cascade.

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. Because these values are all based on ratios there are no values or units, but they give a general idea of a particular relationship. 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, to methylate estrogens very effectively may have positive consequences.

**UPDATE: The DUTCH Complete report now also has a summary page for a quick overview of the most vital information. This includes a screenshot of the reported therapies.**

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 Precision Analytical 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, Precision Analytical removes 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 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.