PRECISION ANALYTICAL
Consulting & Laboratory

Hormone Metabolite Assessment

Accession # 00206213
Anna Salanti
7619 SW 26th Ave
Portland, OR 97219

Ordering physician:
Joel Grimwood

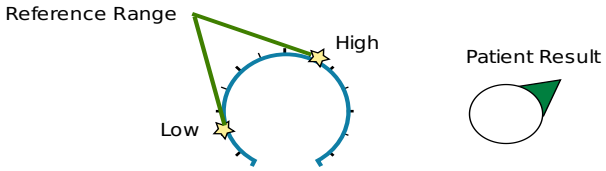
DOB:1952-01-26
Gender: Female

Collection Times:
2014-11-19 05:00PM
2014-11-19 10:00PM
2014-11-20 03:18AM
2014-11-20 08:20AM
2014-11-20 10:30AM

Category	Test		Result	Units	Normal Range
Progesterone Metabolism					
	β-Pregnanediol	Below range	2346.0	ng/mg	2621 - 6826
	α-Pregnanediol	Low end of range	689.0	ng/mg	568 - 1595
Androgen Metabolism					
	DHEAS	Within range	76.0	ng/mg	23 - 252
	Androsterone	Within range	979.0	ng/mg	399 - 1364
	Etiocholanolone	Within range	653.0	ng/mg	371 - 765
	Testosterone	Within range	10.7	ng/mg	5.5 - 17.8
	5α-DHT	Within range	5.0	ng/mg	3.7 - 8.8
	5α-Androstanediol	Within range	42.9	ng/mg	22 - 66
	5β-Androstanediol	High end of range	26.9	ng/mg	6 - 32
	Epi-Testosterone	Low end of range	5.2	ng/mg	4.5 - 22.3
Estrogen Metabolites					
	Estrone(E1)	Above range	48.4	ng/mg	14 - 27.1
	Estradiol(E2)	Above range	7.7	ng/mg	2 - 4.9
	Estriol(E3)	Low end of range	8.7	ng/mg	5.6 - 23
	2-OH-E1	Within range	7.2	ng/mg	4.6 - 14.4
	4-OH-E1	Within range	1.3	ng/mg	0 - 1.8
	16-OH-E1	Within range	2.2	ng/mg	1.3 - 4.6
	2-Methoxy-E1	Within range	4.0	ng/mg	2.9 - 5.9
	2-OH-E2	Within range	0.92	ng/mg	0.4 - 1.2

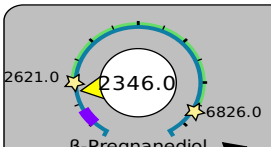
Normal Ranges	Luteal	Postmenopausal	Follicular	Ovulatory
Estrone (E1)	14-27.1	1.3-6.7	4.0-12.0	22-68
Estradiol (E2)	2.0-4.9	0.2-0.8	1.0-2.0	4.0-12.0
Estriol (E3)	5.6-23	0.8-3.7	N/A	N/A
2-OH-E1	4.6-14.4	0.4-1.9	N/A	N/A
4-OH-E1	0-1.8	0-0.3	N/A	N/A
16-OH-E1	1.3-4.6	0.1-	N/A	N/A
2-Methoxy-E1	2.9-5.9	0.2-1.0	N/A	N/A
a-Pregnanediol	80-518	5.0-34	25-100	25-100
b-Pregnanediol	265-1612	28-135	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.

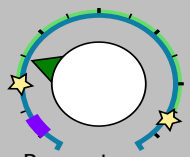


Pregnenolone

Progesterone Metabolism female

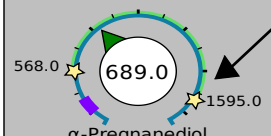


β-Pregnanediol



Progesterone

A weighted average of progesterone metabolites Progesterone itself is not found in urine in measurable levels

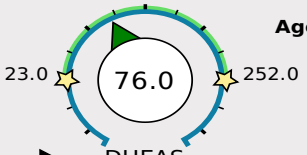


α-Pregnanediol

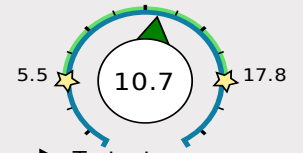
Androgen Metabolism

Age-Dependent DHEAS Ranges

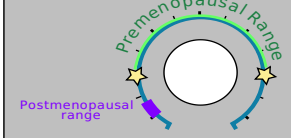
Age	DHEAS
20-40	30-350
40-60	10-100
>60	5-50



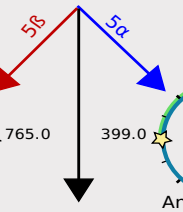
DHEA → DHEAS



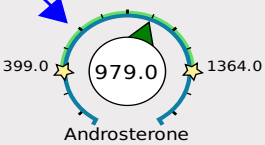
Androstenedione → Testosterone



Androstenedione

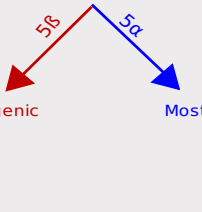


Etiocholanolone



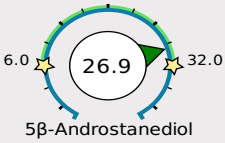
Androsterone

Testosterone

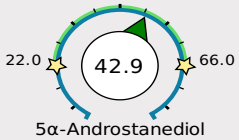


5ß-DHT
Less androgenic

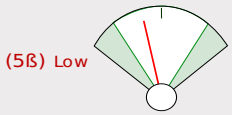
5α-DHT
Most potent androgen



5β-Androstanediol



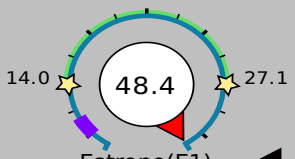
5α-Androstanediol



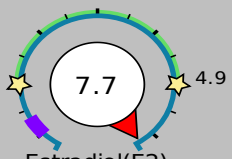
5a-Reductase Activity

5α-Reductase Activity is an overall score of the 5α (more androgenic) vs. 5ß (less androgenic) metabolites of androstenedione and testosterone.

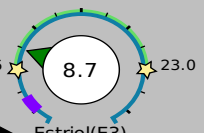
Estrogen Metabolism



Estrone(E1)



Estradiol(E2)



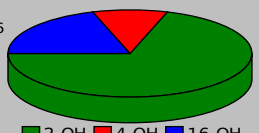
Estriol(E3)

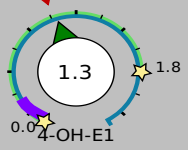
primary estrogens (E1, E2, E3)

protective pathway

16-OH-E1

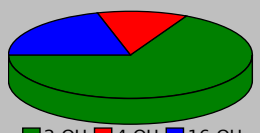
Normal Estrogen Metabolism





4-OH-E1

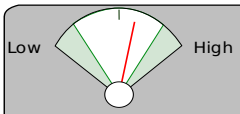
Patient Estrogen Metabolism



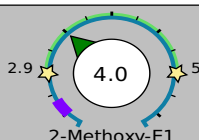
4-Methoxy-E1
(Protective, but not enough in urine to measure)

4-OH-E1

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

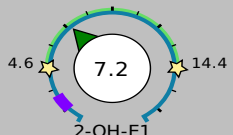


Methylation-activity
(protective)



2-Methoxy-E1

methylation



2-OH-E1

PRECISION ANALYTICAL
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Advanced Adrenal Assessment

Accession # 00206213
Anna Salanti
7619 SW 26th Ave
Portland, OR 97219

Ordering physician:
Joel Grimwood

DOB:1952-01-26
Gender: Female

Collection Times:
2014-11-19 05:00PM
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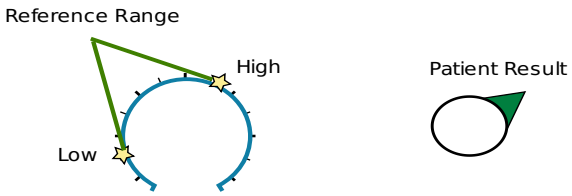
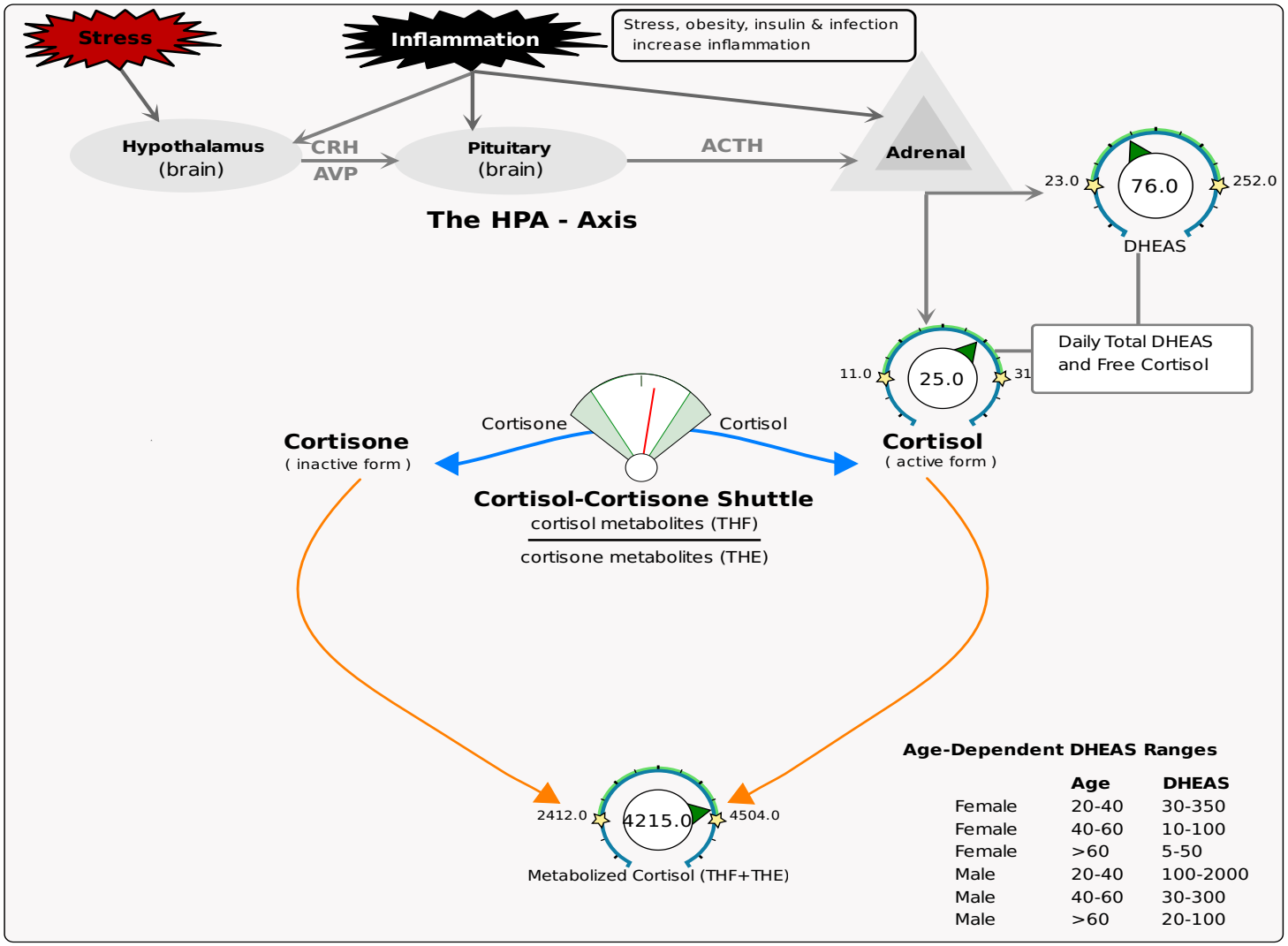
2014-11-20 08:20AM
2014-11-20 10:30AM

Category	Test		Result	Units	Normal Range
Creatinine					
	Creatinine A (Overnight)	Within range	0.58	mg/ml	0.5 - 3
	Creatinine B (Morning)	Within range	0.87	mg/ml	0.5 - 3
	Creatinine C (Afternoon)	Within range	1.19	mg/ml	0.5 - 3
	Creatinine D (Night)	Within range	1.19	mg/ml	0.5 - 3
Daily Free Cortisol and Cortisone					
	Cortisol A	Within range	29.3	ng/mg	10.8 - 39.3
	Cortisol B	Within range	56.2	ng/mg	24.5 - 87
	Cortisol C	High end of range	18.4	ng/mg	6.8 - 20.8
	Cortisol D	Above range	9.4	ng/mg	0 - 7.6
	Cortisone A	Low end of range	49.8	ng/mg	47.2 - 142.9
	Cortisone B	Below range	79.1	ng/mg	103.7 - 267.5
	Cortisone C	Within range	70.5	ng/mg	46.5 - 135.5
	Cortisone D	Within range	30.2	ng/mg	0 - 52.3
	Cortisol-24hr (AUC)	Within range	25.0	ug	11 - 31
	Cortisone-24hr (AUC)	Low end of range	56.0	ug	49 - 131
Cortisol Metabolites and DHEAS					
	b-Tetrahydrocortisol (b-THF)	High end of range	1249.0	ng/mg	783 - 1317
	a-Tetrahydrocortisol (a-THF)	Above range	344.0	ng/mg	134 - 281
	b-Tetrahydrocortisone (b-THE)	High end of range	2622.0	ng/mg	1490 - 2795
	Metabolized Cortisol (THF+THE)	High end of range	4215.0	ng/mg	2412 - 4504
	DHEAS	Within range	76.0	ng/mg	23 - 252
Melatonin (*measured as 6-OH-Melatonin-Sulfate)					
	Melatonin* (Overnight)	Below range	9.768	ng/mg	10 - 50

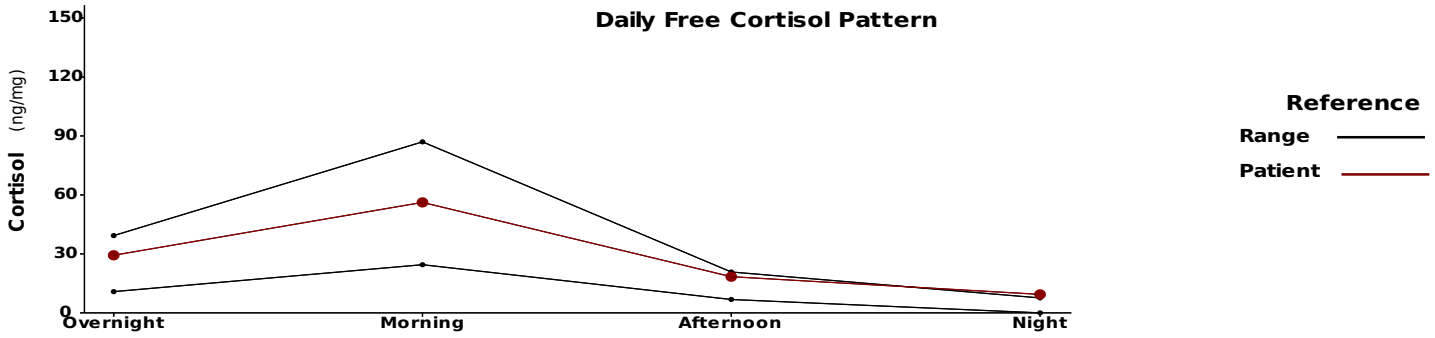
HOW TO READ YOUR RESULTS: Hormones are presented on this page graphically in the order the body metabolizes them. Arrows represent conversion from one hormone to another. The stars represent the low and high limits of the reference ranges (see example, right). The number in the middle is your result.





Age-Dependent DHEAS Ranges

	Age	DHEAS
Female	20-40	30-350
Female	40-60	10-100
Female	>60	5-50
Male	20-40	100-2000
Male	40-60	30-300
Male	>60	20-100



Patient Notes

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.

YOUR REQUISITION FORM MENTIONED AT LEAST ONE HORMONE FOR WHICH YOU DID NOT INFORM THE LAB AS TO HOW (BY WHAT ROUTE OF ADMINISTRATION) YOU TOOK THIS HORMONE. WE CANNOT PROPERLY COMMENT ON HOW RESULTS SHOULD BE INTERPRETTED WITHOUT THIS INFORMATION, SO PLEASE INTERPRET RESULTS CAREFULLY WITH THE HELP OF YOUR PROVIDER.

YOU REPORTED SIGNIFICANT FATIGUE IN THE MORNING, BUT NOT LATER IN THE DAY.

YOU ARE CLASSIFIED AS NONCYCLING BASED ON THE INFORMATION PROVIDED. THE TEST IS STANDARDIZED TO LUTEAL COLLECTIONS (DAYS 19-21 OF THE MENSTRUAL CYCLE) BY CYCLING FEMALES. REFERENCE RANGES FOR NONCYCLING WOMEN FOR PROGESTERONE AND ESTROGEN METABOLITES ARE AS FOLLOWS:

a-Pregnanediol: 5-34ng/mg, b-Pregnanediol: 28-135ng/mg
E1: 1.3-6.7ng/mg, E2: 0.2-0.8ng/mg, E3: 0.8-3.7ng/mg

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.

YOU REPORTED USING ORAL PROGESTERONE. THE REFERENCE RANGES GIVEN ARE SPECIFICALLY FOR CASES WITH ORAL PROGESTERONE AND ASSUME IT WAS TAKEN THE DAY OF THE TEST. URINE METABOLITE VALUES ARE GREATLY INCREASED WITH ORAL PROGESTERONE BECAUSE IT IS HEAVILY METABOLIZED. STUDIES SHOW THAT THE CREATION OF THESE PROGESTERONE METABOLITES RESULTS IN A SIGNIFICANT CLINICAL EFFECT AS THE ENDOMETRIUM IS PROTECTED (WHEN ESTROGEN IS ALSO GIVEN) AND SLEEP DISTURBANCES ARE USUALLY IMPROVED IF TAKEN AT NIGHT.

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.

YOU REPORTED THE USE OF A TESTOSTERONE CREAM OR GEL. THE RESULTS FOR TESTOSTERONE AS WELL AS a-ANDROSTANEDIOL ARE IMPORTANT TO MONITOR WHEN SUPPLEMENTING WITH TESTOSTERONE. YOU WILL WANT TO DISCUSS THESE RESULTS AS WELL AS TESTOSTERONE RELATED SYMPTOMS WITH YOUR PROVIDER. FOR TOPICAL CREAMS URINE TESTING MAY BE SOMEWHAT OF AN UNDERESTIMATION OF EXPOSURE OF SOME TISSUE TO TESTOSTERONE.

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.

YOU NOTED TAKING ORAL ESTROGENS. DEPENDING ON THE TIMING OF YOUR SUPPLEMENTATION AND TESTING YOU MAY HAVE ELEVATED URINE LEVELS THAT DO NOT NECESSARILY REFLECT TOO MUCH ESTROGEN, SO YOU'LL WANT TO DISCUSS THE RESULTS WITH YOUR PROVIDER.

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 morning and fall throughout the day, reaching the lowest point right after going to sleep.

YOUR DAILY PATTERN OF CORTISOL IS RELATIVELY NORMAL EXCEPT FOR A HIGH EVENING CORTISOL. YOU DID NOT REPORT STRESS (STRESS WOULD EXPLAIN THE HIGH LEVELS) DURING THIS TIME PERIOD. YOU MENTIONED HAVING TROUBLE FALLING ASLEEP, SO YOU WILL WANT TO ADDRESS THIS WITH YOUR HEALTH CARE PROVIDER AS HIGH NIGHT CORTISOL MAY PLAY A ROLE IN YOUR SLEEP PROBLEMS.

The daily total of free cortisol is approximated by adding up the four individual measurements of free cortisol. This calculated value correlates closely to a 24-hour free cortisol value.

OVERALL CORTISOL LEVELS ARE APPROPRIATE AS BOTH FREE AND METABOLIZED CORTISOL LEVELS ARE WITHIN RANGE. IF THE DAILY PATTERN OF FREE CORTISOL IS AS EXPECTED, THIS IMPLIES NORMAL HPA-AXIS CORTISOL PRODUCTION.

The Cortisol-Cortisone Shuttle: Cortisol, which is the active hormone, can convert into cortisone, the inactive form. They "shuttle" 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 coritsone 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.

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.

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.

Provider Notes

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 4/4/2013.
Click here to see a video to assist in how to read the report

THE PATIENT MENTIONED TAKING ONE HORMONE FOR WHICH THEY DID NOT LIST THE ROUTE OF ADMINISTRATION (ROA). THE ROA CAN HAVE PROFOUND EFFECT ON EXPECTED RESULTS, AND YOU MAY WANT TO CHECK THE ATTACHED REQUISITION (IN THE ONLINE PORTAL) TO VIEW WHICH HORMONE WAS NOT LISTED PROPERLY. IF YOU WISH FOR AN UPDATED REPORT WITH THE INFORMATION CORRECTED, PLEASE CONTACT THE LAB.

THE PATIENT IS EXPERIENCING SIGNIFICANT FATIGUE IN THE MORNINGS

YOUR PATIENT IS CLASSIFIED AS NONCYCLING. THE TEST IS STANDARDIZED TO LUTEAL COLLECTIONS BY CYCLING FEMALES. REFERENCE RANGES FOR NONCYCLING WOMEN FOR PROGESTERONE AND ESTROGEN METABOLITES ARE AS FOLLOWS:

a-Pregnanediol: 5-34ng/mg, b-Pregnanediol: 28-135ng/mg
E1: 1.3-6.7ng/mg, E2: 0.2-0.8ng/mg, E3: 0.8-3.7ng/mg

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.

THE PATIENT REPORTS USE OF ORAL PROGESTERONE. RESULTS ARE REPORTED RELATIVE TO A REFERENCE RANGE FOR INDIVIDUALS TAKING ORAL PROGESTERONE (100MG). THIS ASSUMES IT WAS TAKEN THE DAY/NIGHT OF TESTING AND NOT SKIPPED. 100MG OF ORAL PROGESTERONE TYPICALLY RESULTS IN URINE METABOLITE VALUES WELL ABOVE THE PREMENOPAUSAL REFERENCE RANGE (WHICH IS 265-1612 FOR b-PREGNANEDIOL). LEVELS OF b-PREGNANEDIOL CORRELATE WITH SERUM PROGESTERONE WHEN WOMEN ARE NOT SUPPLEMENTING. WITH ORAL PROGESTERONE, THE METABOLITES MEASURED INCREASE TO A MUCH GREATER DEGREE THAN SERUM PROGESTERONE LEVELS (SERUM PROGESTERONE LEVELS DO NOT RAISE ABOVE 2NG/ML IN MOST STUDIES WITH ACCURATE MEASUREMENTS). STUDIES SHOW THAT THE CREATION OF THESE PROGESTERONE METABOLITES RESULTS IN A SIGNIFICANT CLINICAL EFFECT AS THE ENDOMETRIUM IS PROTECTED (WHEN ESTROGEN IS CONCURRENTLY GIVEN) AND SLEEP DISTURBANCES ARE USUALLY IMPROVED (BECAUSE OF LARGE AMOUNTS OF THE ALLO-PREGNANOLONE METABOLITE). IT MAY BE THAT WOMEN RESPOND DIFFERENTLY TO ORAL PROGESTERONE DEPENDING ON HOW MUCH OF IT GETS METABOLIZED DOWN THE MORE BIOLOGICALLY ACTIVE a-PATHWAY.

SERUM PROGESTERONE LEVELS DO NOT INCREASE MUCH BECAUSE THE HORMONE IS SO EXTENSIVELY METABOLIZED IN THE GUT. IF YOU DESIRE TO INCREASE SERUM PROGESTERONE LEVELS, A DIFFERENT ROUTE OF ADMINISTRATION (VAGINAL, SUBLINGUAL) SHOULD BE USED.

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-androstanediol within target tissues and then excreted. As such, a-androstanediol may best represents 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.

THE PATIENT REPORTS USE OF TRANSDERMAL TESTOSTERONE. EXPECTED LEVELS WITH TOPICAL HORMONES ARE CONTRAVERSIAL AND NOT ENTIRELY CLEAR. SOME TISSUE (THE SALIVA GLAND BEING ONE EXAMPLE) GET MORE TESTOSTERONE THAN IMPLIED BY URINE OR SERUM VALUES.

50MG OF TESTOSTERONE (A TYPICAL DOSE IN MEN) RAISES SALIVA VALUES MORE THAN 1500% ABOVE BASELINE, A HUGE INCREASE. ALL TISSUES DO NOT SHOW THIS INCREASE. SERUM AND URINE LEVELS INCREASE MARGINALLY WITH THESE DOSES AND CLINICAL STUDIES SHOW THAT MUSCLE MASS INCREASE IS MODEST WITH 50MG (IN MEN) AND ONLY IF SERUM LEVELS INCREASE SIGNIFICANTLY. LH VALUES ARE ONLY PARTIALLY SUPPRESSED WITH THESE DOSES, SO IT IS CLEAR THAT SALIVA VALUES OVERESTIMATE SYSTEMIC TESTOSTERONE EXPOSURE. WHEN TISSUE ARE EXPOSED TO TESTOSTERONE, SOME OF IT WILL BE CONVERTED TO a-DHT AND THEN TO a-ANDROSTANEDIOL WITHIN THE TARGET CELL. a-ANDROSTANEDIOL MAY WELL BE THE BEST MARKER FOR OVERALL ANDROGENICITY FOLLOWING TOPICAL TESTOSTERONE SUPPLEMENTATION ALTHOUGH IN URINE IT IS ALSO A METABOLITE OF DHEAS.

TOPICAL GELS MAY RESULT IN HIGHER VALUES THAN CREAMS.

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.

THE PATIENT NOTED TAKING ORAL ESTROGENS. INSTRUCTIONS ADVISE AVOIDING TAKING THE ESTROGEN ON THE DAY OF TESTING TO AVOID FIRST-PASS METABOLISM. IF THE SUPPLEMENT IS TAKEN THE DAY OF TESTING, RESULTS WILL LIKELY BE ELEVATED DUE TO SIGNIFICANT FIRST-PASS METABOLISM. ADJUSTING DOSING BASED ON THESE NUMBERS IS NOT ADVISABLE, BUT THE METABOLISM PATTERNS ARE USEFUL.

ASSUMING INSTRUCTIONS ARE FOLLOWED, ABSOLUTE VALUES OF ESTROGENS AS WELL AS METABOLISM PATTERNS ARE USEFUL ALTHOUGH IT IS NOT KNOWN WITH CERTAINTY HOW LONG IT TAKES TO ENSURE THAT MEASUREMENTS INCLUDE CIRCULATING ESTROGENS ONLY AND NOT FIRST-PASS METABOLITES. IF E1 AND E2 VALUES ARE ELEVATED AND 2,4, AND 16-OH ESTROGENS ARE NOT, THESE METABOLITES MAY BETTER REFLECT SYSTEMIC ESTROGENS AND E1 AND E2 MAY BE ELEVATED DUE TO FIRST-PASS EFFECTS.

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 patters 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 cortisol awakening response is somewhat independent of the natural diurnal pattern and happens rather quickly (within 10 minutes of waking).

THE PATIENT'S DIURNAL PATTERN OF CORTISOL IS RELATIVELY NORMAL EXCEPT FOR A HIGHER THAN EXPECTED EVENING CORTISOL. THE PATIENT DID NOT REPORT STRESS DURING THIS TIME. THE PATIENT REPORTED TROUBLE FALLING ASLEEP, SO THIS ELEVATION IS WORTH ADDRESSING AS IT RELATES TO SLEEP.

The daily total of free cortisol is approximated by integrating the area under the daily free cortisol curve from the four individual measurements of free cortisol. This calculated value correlates closely 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.

OVERALL CORTISOL LEVELS ARE APPROPRIATE AS BOTH FREE AND METABOLIZED CORTISOL LEVELS ARE WITHIN RANGE. IF THE DIURNAL PATTERN OF FREE CORTISOL IS AS EXPECTED, THIS IMPLIES NORMAL HPA-AXIS CORTISOL PRODUCTION.

Cortisol-Cortisone Shuttle: The back-and-forth conversion of cortisol and 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 cortisol-cortisone shuttle gauge 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.

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.

What is actually measured in urine? In blood, most hormones are bound to binding poteins. 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.