PRECISION ANALYTICAL
Consulting & Laboratory

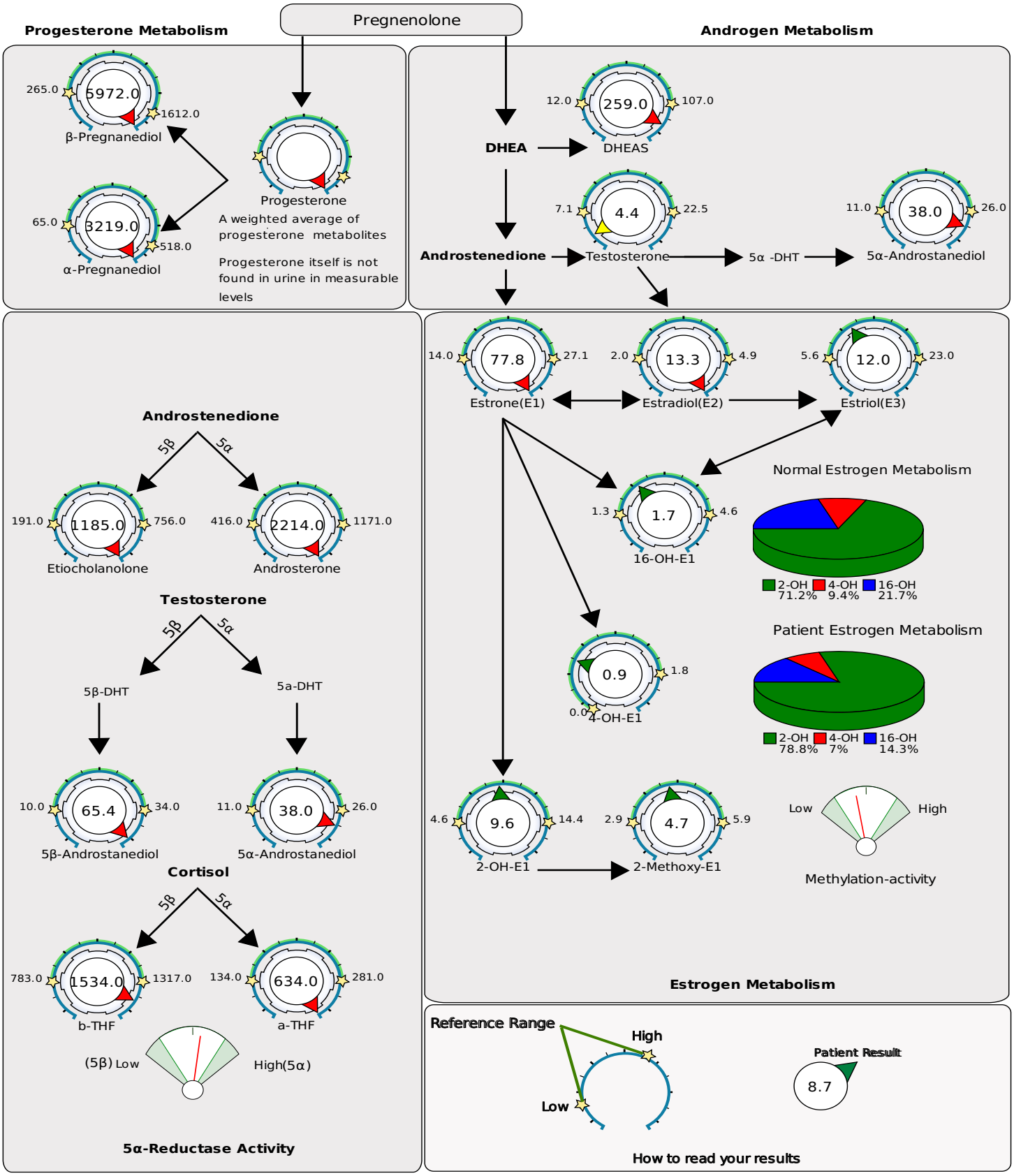
Accession # 00200104
Anna Salanti
7619 SW 26th Ave
Portland, OR 97219

Ordering physician:
Mark Schauss

DOB:1952-01-26
Gender: Female

Collection Times:
2013-02-10 05:01PM
2013-02-10 10:34PM
2013-02-11 05:32AM
2013-02-11 07:31AM

Category	Test		Result	Units	Normal Range
Progesterone Metabolism					
	β-Pregnanediol	Above range	5972.0	ng/mg	265 - 1612
	α-Pregnanediol	Above range	3219.0	ng/mg	65 - 518
	Pregnenediol	Within range	2.16	ng/mg	0 - 5.19
Androgen Metabolism					
	Androsterone	Above range	2214.0	ng/mg	416 - 1171
	Etiocholanolone	Above range	1185.0	ng/mg	191 - 756
	Testosterone	Below range	4.4	ng/mg	7.1 - 22.5
	5α-DHT	Within range	6.3	ng/mg	2.8 - 7.2
	5α-Androstanediol	Above range	38.0	ng/mg	11 - 26
	5β-DHT	Above range	8.4	ng/mg	0 - 2.2
	5β-Androstanediol	Above range	65.4	ng/mg	10 - 34
	Epi-Testosterone	Below range	2.1	ng/mg	8.5 - 18.9
Estrogen Metabolites					
	Estrone(E1)	Above range	77.8	ng/mg	14 - 27.1
	Estradiol(E2)	Above range	13.3	ng/mg	2 - 4.9
	Estriol(E3)	Within range	12.0	ng/mg	5.6 - 23
	2-OH-E1	Within range	9.6	ng/mg	4.6 - 14.4
	4-OH-E1	Within range	0.9	ng/mg	0 - 1.8
	16-OH-E1	Low end of range	1.7	ng/mg	1.3 - 4.6
	2-Methoxy-E1	Within range	4.7	ng/mg	2.9 - 5.9
	4-Methoxy-E1	Within range	0.2	ng/mg	0 - 0.3
	2-OH-E2	High end of range	1.17	ng/mg	0.4 - 1.2
	2-Methoxy-E2	Within range	0.13	ng/mg	0 - 0.2


Pregnenolone
Progesterone Metabolism
Androgen Metabolism
265.0
5972.0
1612.0
β-Pregnanediol
Progesterone
A weighted average of progesterone metabolites
Progesterone itself is not found in urine in measurable levels
65.0
3219.0
518.0
α-Pregnanediol
12.0
259.0
107.0
DHEA
DHEAS
7.1
4.4
22.5
Androstenedione
Testosterone
5α -DHT
11.0
38.0
26.0
5α-Androstanediol
14.0
77.8
27.1
Estrone(E1)
2.0
13.3
4.9
Estradiol(E2)
5.6
12.0
23.0
Estriol(E3)
Normal Estrogen Metabolism
1.3
1.7
4.6
16-OH-E1
2-OH 71.2%
4-OH 9.4%
16-OH 21.7%
Patient Estrogen Metabolism
0.9
1.8
0.0
4-OH-E1
2-OH 78.8%
4-OH 7%
16-OH 14.3%
4.6
9.6
14.4
2-OH-E1
2.9
4.7
5.9
2-Methoxy-E1
Low
High
Methylation-activity
Estrogen Metabolism
Androstenedione
5β
5α
191.0
1185.0
756.0
Etiocholanolone
416.0
2214.0
1171.0
Androsterone
Testosterone
5β
5α
5β-DHT
5a-DHT
10.0
65.4
34.0
5β-Androstanediol
11.0
38.0
26.0
5α-Androstanediol
Cortisol
5β
5α
783.0
1534.0
1317.0
b-THF
134.0
634.0
281.0
a-THF
(5β) Low
High(5α)
5α-Reductase Activity
Reference Range
High
Low
Patient Result
8.7
How to read your results

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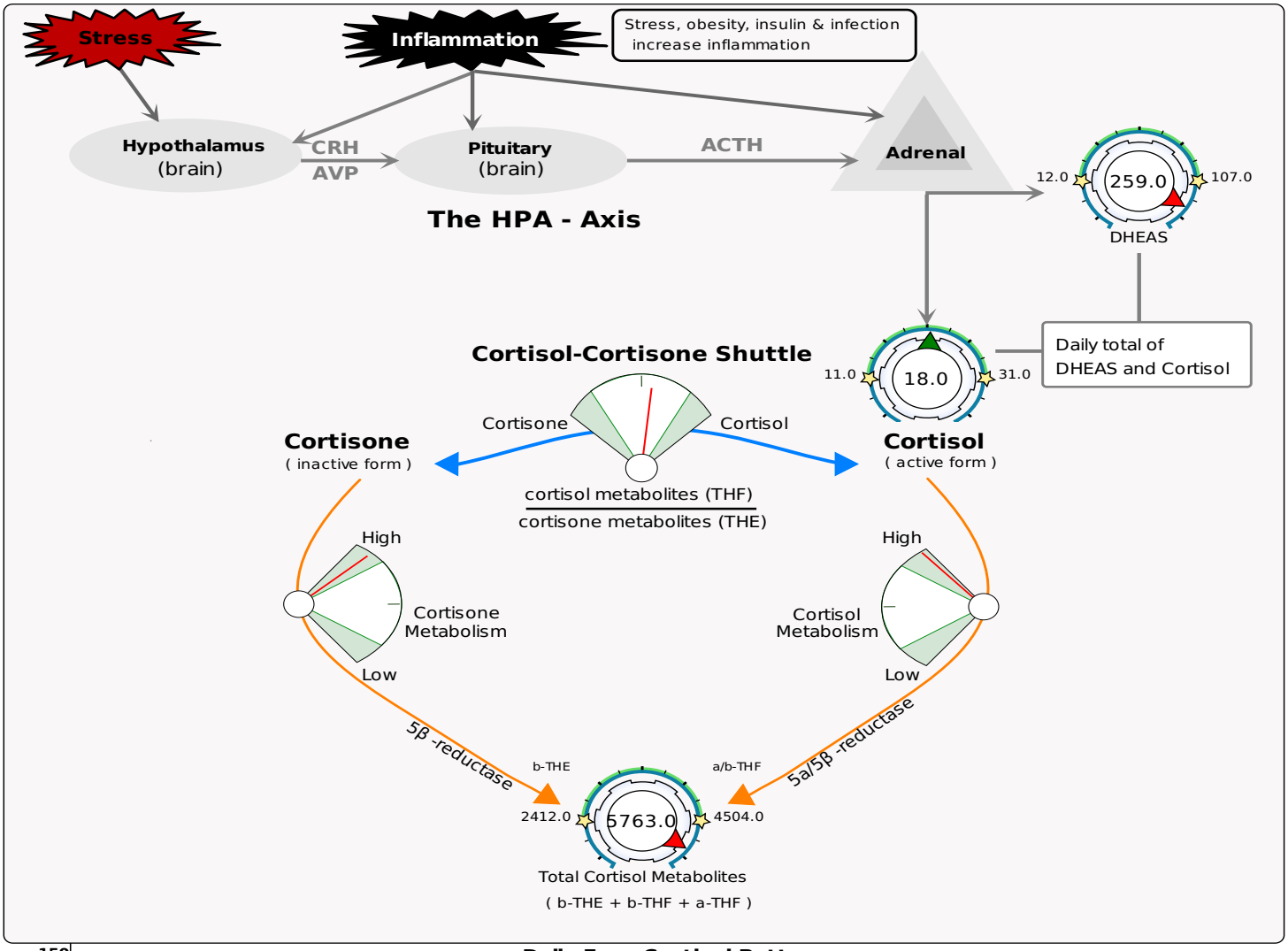
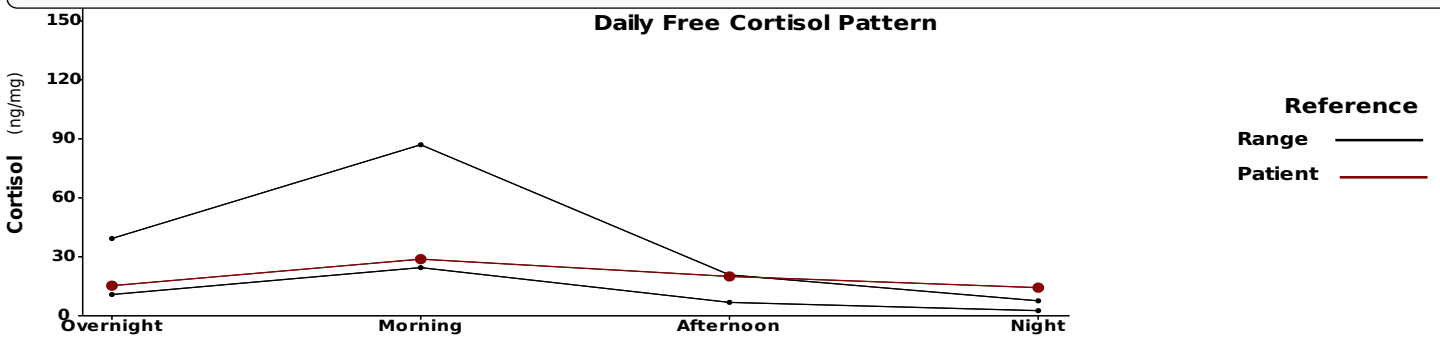
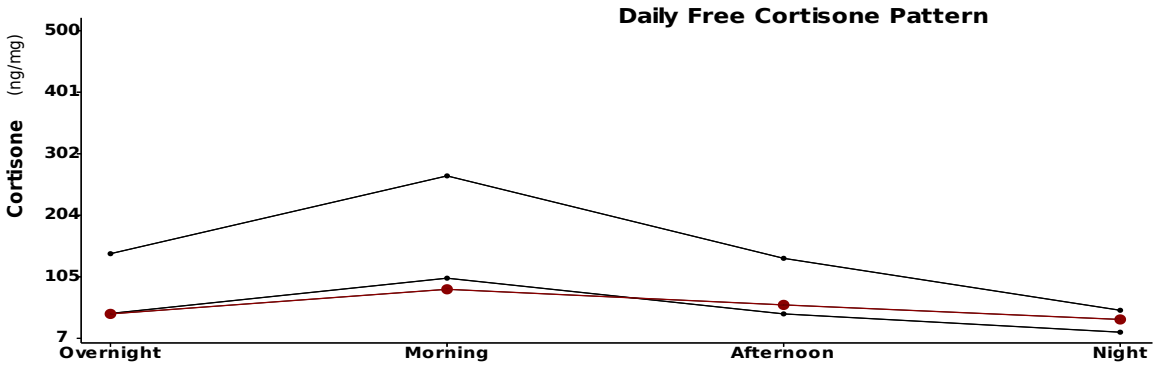
Collection Times:
2013-02-10 05:01PM
2013-02-10 10:34PM
2013-02-11 05:32AM
2013-02-11 07:31AM

Category	Test		Result	Units	Normal Range
Creatinine					
	Creatinine A (Overnight)	Within range	0.96	mg/ml	0.5 - 3
	Creatinine B (Morning)	Within range	1.09	mg/ml	0.5 - 3
	Creatinine C (Afternoon)	Within range	0.6	mg/ml	0.5 - 3
	Creatinine D (Night)	Within range	0.77	mg/ml	0.5 - 3
Daily Free Cortisol and Cortisone					
	Cortisol A	Low end of range	15.3	ng/mg	10.8 - 39.3
	Cortisol B	Low end of range	28.8	ng/mg	24.5 - 87
	Cortisol C	High end of range	20.0	ng/mg	6.8 - 20.8
	Cortisol D	Above range	14.3	ng/mg	2.6 - 7.6
	Cortisone A	Below range	46.5	ng/mg	47.2 - 142.9
	Cortisone B	Below range	85.9	ng/mg	103.7 - 267.5
	Cortisone C	Low end of range	60.9	ng/mg	46.5 - 135.5
	Cortisone D	Within range	37.6	ng/mg	17.2 - 52.3
	Cortisol-24hr (AUC)	Within range	18.0	ug	11 - 31
	Cortisone-24hr (AUC)	Low end of range	54.0	ug	49 - 131
Cortisol Metabolites and DHEAS					
	b-Tetrahydrocortisol (b-THF)	Above range	1534.0	ng/mg	783 - 1317
	a-Tetrahydrocortisol (a-THF)	Above range	634.0	ng/mg	134 - 281
	b-Tetrahydrocortisone (b-THE)	Above range	3595.0	ng/mg	1490 - 2795
	Total Cortisol Metabolites	Above range	5763.0	ng/mg	2412 - 4504
	DHEAS	Above range	259.0	ng/mg	12 - 107


Stress
Inflammation
Stress, obesity, insulin & infection increase inflammation
Hypothalamus (brain)
CRH
AVP
Pituitary (brain)
ACTH
Adrenal
The HPA - Axis
12.0
259.0
107.0
DHEAS
Daily total of DHEAS and Cortisol
Cortisol-Cortisone Shuttle
11.0
18.0
31.0
Cortisone
Cortisol
Cortisone (inactive form)
Cortisol (active form)
cortisol metabolites (THF)
cortisone metabolites (THE)
High
Low
Cortisone Metabolism
Cortisol Metabolism
5β -reductase
5a/5β -reductase
b-THE
a/b-THF
2412.0
6763.0
4504.0
Total Cortisol Metabolites
(b-THE + b-THF + a-THF)


Daily Free Cortisol Pattern
Cortisol (ng/mg)
150
120
90
60
30
0
Overnight
Morning
Afternoon
Night
Reference
Range
Patient


Daily Free Cortisone Pattern
Cortisone (ng/mg)
500
401
302
204
105
7
Overnight
Morning
Afternoon
Night

Patient Notes

Thank you for testing with Precision Analytical, Inc. Due to the complexity of the analysis, you will need the guidance of your health care provider in order to properly interpret your results. The information here is intended to assist you in understanding your results in conjunction with your visit with your provider. You may want to skip to the last two paragraphs first for an explanation of how to read the report and background information on urine hormone testing before continuing with the report. You should 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 back to your provider.

Progesterone Background: This hormone is made (by the corpus luteum of the ovary) in high concentrations in women directly following successful ovulation and in even higher levels during pregnancy. Small amounts are made in other parts of the body, so some progesterone is found in women who have not recently ovulated (postmenopausal, on birth control pills, first 14 days of the cycle). The primary role of progesterone is to balance the strong effects of estrogen. High levels of estrogen without the presence of adequate progesterone can increase risks for some cancers, premenstrual syndrome (PMS) and other symptoms associated with excess estrogen.

Progesterone Metabolism: Because progesterone does not readily form phase II metabolites (conjugates), very little is found in urine. Instead, the most abundant metabolites are used to track progesterone levels. This main metabolite is known as pregnanediol. Usually labs measure only b-pregnanediol, but we also measure a-pregnanediol. Your result for progesterone (on page 2) is a weighted average of these two metabolites. Both metabolites should go up and down with blood progesterone levels, but an average of the two is a better index of progesterone status than either metabolite as a single marker. The middle of the gauge (an average value) would most likely represent an average progesterone level in the blood (10-15ng/ml) if you were to compare. The reference range for progesterone is extended a little more than other hormones on the high end as slightly elevated progesterone is not generally associated with negative consequences.

YOU REPORTED USING ORAL PROGESTERONE. RESULTS MUST BE INTERPRETED CAREFULLY. 100MG OF ORAL PROGESTERONE (A COMMON DOSE) TYPICALLY RESULTS IN URINE METABOLITE VALUES WELL ABOVE THE REFERENCE RANGE (2-5 TIMES HIGHER). ELEVATED RESULTS IN THIS CASE DO NOT NECESSARILY IMPLY TOO MUCH HORMONE HAS BEEN GIVEN. 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 Background: This group of hormones is typically thought of as “male” hormones, but they play a key role for women as well. The ovaries make the primary androgen testosterone as well as others. The adrenal glands also contribute by making DHEA, DHEA-S, and androstenedione, weaker androgens and precursors to testosterone. Androgens generally contribute to attributes that are typically more pronounced in males than females (general and sexual aggression, muscle mass, increased facial/body hair, reduction of fat deposition, etc). Testosterone deficiency can lead to decreased sexual function, vaginal dryness, and bone loss. As females transition through menopause and their ovaries cease to function properly, their testosterone can also drop (use of birth control bills is another common cause of low testosterone in women).

Androgen Metabolism: Urine metabolites offer a lot of information about androgen metabolism, but it can be somewhat complicated. a-DHT (a-dihydrotestosterone) is the most potent androgen (3 times more potent than testosterone). While we do report a-DHT levels, a-androstanediol actually best represents a=DHT even though a-DHT is more biologically active and well known. The beta (b) metabolites (i.e. b-DHT) are not androgenic however we report both 5a and 5b-pathway metabolites to properly assess how testosterone is being metabolized.
Androgens are the immediate precursor to estrogens so assessing metabolism also includes looking at how much androstenedione and testosterone gets turned into estrogen. The enzyme responsible for this transition (aromatase) exists in the ovaries, but also in fat cells and other places in the body.

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). These enzymes also metabolize progesterone and cortisol. The alpha metabolites of androstenedione and testosterone (such as a-DHT) are far more potent than their beta counterparts (such as b-DHT). As a result, increased 5a-reductase enzyme activity may be accompanied by clinical signs of high androgens such as excess facial hair growth, scalp hair loss, acne, irritability and oily skin.

YOU REPORTED USING ORAL DHEA. FOR WOMEN, DHEA WILL OFTEN INCREASE BOTH TESTOSTERONE AND ESTROGEN LEVELS. IN MEN THE METABOLISM IS SOMETIMES LESS FAVORABLE SHIFTING MORE TOWARDS

ESTROGENS THAN IS IDEAL. YOU WILL WANT TO CAREFULLY EXAMINE ANDROGENS AND ESTROGENS WITH ORAL DHEA THERAPY TO SEE HOW IT IS BEING METABOLIZED.

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.

Estrogen Background: Before ovulation, a female's estrogen levels are about the same as those found in men and postmenopausal women. There is a surge of estrogen around ovulation (day 14) followed by a plateau around days 19-21, which is when testing is most relevant for premenopausal women. During this part of the menstrual cycle, women make about three times more estrogen than a man. The primary role of estrogen is in the development of female sexual characteristics and reproduction.

Estrogen Metabolism: There are three types of estrogen. Estradiol (E2) is the most potent and common during the reproductive years and can be converted into estrone (E1) and estriol (E3). When it comes to testing hormones, it is important to look at your actual estrogen production (are you deficient, sufficient or in excess?) and how you metabolize your estrogen through the liver (hydroxylation and methylation). All estrogen ranges are based on mid-luteal (days 19-21 of a typical 28-day menstrual cycle) collections for females.

YOU REPORTED USING ORAL ESTROGEN. WHEN YOU TAKE ESTROGEN ORALLY A GREAT DEAL OF IT ENDS UP GETTING METABOLIZED AND EXCRETED IN URINE BEFORE HAVING ANY EFFECT. RESULTS OF ESTROGEN METABOLITES (ESPECIALLY ESTRONE AND ESTRADIOL) ARE OFTEN HIGH WITH ORAL SUPPLEMENTATION, BUT THIS DOES NOT NECESSARILY MEAN TOO MUCH ESTROGEN HAS BEEN GIVEN. THE WAY THIS ESTROGEN IS METABOLIZED IS IMPORTANT AND YOU MAY WANT TO DISCUSS THOSE PATTERNS WITH YOUR PROVIDER.

Estrogen Hydroxylation: Hydroxylation occurs in the liver during phase I detoxification. Both estradiol and estrone can be hydroxylated by three competing enzymes. One enzyme creates 2-OH-Estrone (2OH-E1) and 2-OH-Estradiol (2OH-E2) that are known for their protective effects within the body. Another creates 16-OH-Estrone (16OH-E1) and 16-OH-Estradiol (estriol) and a third makes the potentially cancer-causing 4-OH-Estrone (4OH-E1) and 4-OH-Estradiol (4OH-E2). These three competing pathways can be shown with the pie chart on the report. Imbalances can be addressed through specific dietary changes and supplements. This may help reduce the risk of estrogen-mediated cancers.

2-OH and 4-OH Estrogen Methylation: Once hydroxylated estrogens have been formed, the 2 and 4-OH estrogens can be further metabolized by the liver through methylation. If they are successfully methylated, they can be excreted in the urine without causing any harm to your body. If they are not methylated, these reactive estrogens can cause problems with your DNA building blocks. The 4-OH estrogens do this in a manner that is far worse than the 2-OH estrogens, which is why the 4-OH estrogens are considered carcinogens. 2-OH estrogens do cause problems with your DNA but show an overall anti-estrogenic effect that may in fact be protective to your body. On your results, the methylation efficiency is assessed by looking at the relationship between your 2-OH-E1 and the corresponding 2-Methoxy-E1.

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.

OVERALL FREE CORTISOL LEVELS ARE WITHIN THE EXPECTED RANGE. SINCE YOU REPORTED HIGH LEVELS OF STRESS THE DAY OF COLLECTION, THERE COULD BE SOME CONCERN THAT "NORMAL" LEVELS OF THE STRESS HORMONES REPRESENT AN INADEQUATE ADRENAL RESPONSE TO STRESS.

The Cortisol-Cortisone Shuttle: Cortisol, which is the active hormone, can convert into cortisone, the inactive hormone, in the body for both normal and abnormal reasons. This back-and-forth shuttle happens in different organs and tissues by two forms of the enzyme 11b-HSD. The inactivation of cortisol to cortisone happens mainly in the kidneys and colon (11b-HSD II). On the other hand, the activation of cortisone to cortisol (11b-HSD I) happens mainly in the liver, adipose (fat) tissue, gonads, brain and muscle. Most cortisol ends up in urine as tetrahydrocortisol (a-THF, b-THF), and most cortisone ends up excreted in urine as tetrahydrocortisone (b-THE). Research shows that the best way to determine the body's overall balance between cortisol and cortisone is to look at the relationship between these end metabolites (instead of looking directly at cortisol and cortisone). Increasing the preference for cortisone can be helpful in individuals with conditions related to excessive cortisol. Likewise, increasing cortisol production can help in situations where cortisol is low.

THE RATIO BETWEEN YOUR THF/THE SHOWS A MODEST PREFERENCE FOR CORTISOL. THIS IS CONFIRMED BY THE FACT THAT YOUR RATIO OF FREE CORTISOL COMPARED TO FREE CORTISONE IS ALSO HIGH (COMPARED TO THE EXPECTED VALUES). WHEN LOOKING AT YOUR HEIGHT COMPARED TO YOUR WEIGHT ON THE BODY-MASS-INDEX CHART (BMI), YOUR BMI IS HIGH AND HAVING EXCESS CENTRAL ADIPOSITY (BELLY FAT) MAY BE SOMEWHAT DUE TO THIS PREFERENCE FOR CORTISOL. IN ADDITION, THE ENZYME THAT CONVERTS CORTISONE INTO CORTISOL IS MORE ACTIVE IN FAT TISSUE CAUSING HIGHER CORTISOL

LEVELS.

Cortisol Metabolism: The conversion of cortisol to cortisone (and vice versa) is reversible. The conversion of cortisol or cortisone to their inactive metabolites (a-THF, b-THF, b-THE) is not. Therefore, once cortisol turns into THF (and cortisone into THE) there is no way to go back. The conversion to these metabolites happens mainly in the liver through the enzymes 5a-reductase and 5b-reductase. When one or both of these enzymes is turned up, there can be a cortisol deficiency even though the adrenal glands are making significant amounts of cortisol. This hyper-conversion of cortisol happens commonly in long-term stress, obesity, insulin resistance, and hyperthyroidism. Measuring both the cortisol/cortisone and their metabolites is important to understand what is truly happening in the body. Fatigue and other conditions related to low cortisol can be caused by an adrenal gland that is not producing enough cortisol or by excessive metabolism.

WHEN YOU ARE STRESSED FOR A LONG PERIOD OF TIME, THE ENZYMES THAT METABOLIZE CORTISOL GET TURNED UP. YOUR CORTISOL IS NOT ELEVATED, BUT YOUR CORTISOL METABOLISM RATES ARE QUITE HIGH. THIS IS OFTEN A PICTURE OF LONG-TERM STRESS. OBESITY AND INSULIN RESISTANCE ARE OTHER COMMON CAUSES OF INCREASED METABOLISM RATES. AS THIS EXCESS METABOLISM GETS WORSE, THE ADRENAL GLAND MAY TIRE AND HAVE TROUBLE PRODUCING ENOUGH CORTISOL. TAKING EFFORTS TO KEEP YOUR HPA-AXIS FROM BEING CHRONICALLY TURNED UP SEEMS IN ORDER, AND YOU MAY WANT TO DISCUSS THIS WITH YOUR HEALTH CARE PROVIDER.

The Daily Free Cortisol Pattern: The primary reason for the timing of the urine collections for this test is to assess the daily pattern of cortisol (and to a lesser extent cortisone). Typical urine testing (ex. The 24-hour collection) averages the daily production of cortisol into one grand total but does not take into account the levels in the morning compared to the evening. Dysfunctional daily patterns have been associated health-related problems such as fatigue. While the daily pattern of cortisol is of primary interest in this report, the cortisone pattern may provide additional clarity in certain situations. Remember that free cortisol levels should be the highest in the morning sample and progressively lower for the next two samples. Because cortisol levels start to creep up after about 1am, the overnight sample is typically somewhere between the evening and bedtime samples and may be elevated in people with sleep problems.

YOUR DAILY PATTERN OF CORTISOL IS SIGNIFICANTLY DISTURBED AS YOUR LEVELS WERE LOW IN THE MORNING AND ELEVATED IN THE AFTERNOON/EVENING WHICH IS THE OPPOSITE OF EXPECTED PATTERNS. THIS MAY BE CONTRIBUTING TO YOUR REPORTED FATIGUE SYMPTOMS, ESPECIALLY IN THE MORNING. HIGH LEVELS OF STRESS WERE REPORTED IN THIS TIME PERIOD, SO THE ELEVATED CORTISOL MAY BE DUE TO AN IMMEDIATE STRESSOR (SUCH AS AN EVENT, INTERACTION OR PAIN) AND THE CORTISOL PATTERN MAY ACTUALLY BE LOW ALL DAY IF THIS IMMEDIATE STRESSOR DID NOT OCCUR. IF THIS IMMEDIATE STRESSOR DOES OCCUR DAILY, THEN THE ELEVATED CORTISOL LEVEL IS YOUR ACTUAL RESPONSE. STRESS REDUCTION MAY HELP ELIMINATE THE ELEVATED CORTISOL LATE IN THE DAY, AND YOU MAY WANT TO DISCUSS STRATEGIES TO ADDRESS THE LOW MORNING ADRENAL RESPONSE WITH YOUR HEALTH CARE 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. 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.

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. 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.

Progesterone Metabolism: Because progesterone does not readily form phase II metabolites, very little is found in urine. b-Pregnanediol is typically used a surrogate marker because it is the most abundant metabolite. This metabolite is found in the 5b-reductase pathway and a better overall representation of progesterone can be found if the 5a-reductase metabolite (a-pregnanediol) is also measured. The graphical representation of progesterone (on page 2) is a weighted average of these two metabolites. Both metabolites should go up and down with serum progesterone levels, but an average of the two is a better index of progesterone status than either metabolite as an independent marker. This index should parallel serum progesterone levels. The middle of the gauge (an average value) likely represents a serum progesterone level of about 10-15ng/ml.

The upper end of the range for most hormones is the 80th percentile of young, healthy individuals. For progesterone and its metabolites, this range is extended to the 90th percentile because slightly elevated progesterone is not generally associated with negative consequences.

THE PATIENT REPORTS USE OF ORAL PROGESTERONE. RESULTS MUST BE INTERPRETED CAREFULLY. 100MG OF ORAL PROGESTERONE TYPICALLY RESULTS IN URINE METABOLITE VALUES WELL ABOVE THE PREMENOPAUSAL REFERENCE RANGE (2-5 TIMES HIGHER). ELEVATED RESULTS IN THIS CASE DO NOT NECESSARILY IMPLY TOO MUCH HORMONE HAS BEEN GIVEN. 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).

BE ADVISED, HOWEVER, THAT THESE LEVELS DO NOT IMPLY PREMENOPAUSAL LEVELS OF SERUM PROGESTERONE. 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: Urine metabolites offer a lot of information about androgen metabolism, but it can be somewhat complicated. 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 conjugated (glucuronidation) for excretion. As such, it is a-androstanediol that 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.

a-DHT levels can be increased if testosterone levels are increased, or by a change in the activity of the enzyme 5a-reductase (relative to 5b-reductase, which makes 5b-DHT). To assess this complex issue, we report both 5a and 5b-pathway metabolites for consideration.

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). It is important to note that one of the most relevant 5a-reductase products, a-DHT, is formed in significant amounts within target tissues (making a-DHT a paracrine hormone) from testosterone. This means that the relative activity between the two enzymes may be somewhat unique for testosterone metabolism (compared to androstenedione and cortisol metabolism, which is mostly in the liver). 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).

THE PATIENT REPORTS USE OF ORAL DHEA. FOR WOMEN, DHEA WILL OFTEN INCREASE BOTH TESTOSTERONE AND ESTROGEN LEVELS. IN MEN THE METABOLISM IS SOMETIMES LESS FAVORABLE SHIFTING MORE TOWARDS ESTROGENS THAN IS IDEAL. YOU WILL WANT TO CAREFULLY EXAMINE ANDROGENS AND ESTROGENS WITH ORAL

DHEA THERAPY. THE DHEA MEASURED IN URINE IS PRIMARILY DHEA-S. DHEA CAN INCREASE DOWNSTREAM METABOLITES SIGNIFICANTLY WITHOUT NECESSARILY INCREASING DHEA-S BY THE SAME DEGREE. FREE DHEA IS NOT REPORTED BUT THE ANDROSTENEDIONE METABOLITES (ANDROSTERONE, ETIOCHOLANOLONE) MAY PARALLEL DHEA LEVELS.

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. PAY SPECIAL ATTENTION TO THIS METABOLITE.

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?) Urine testing can be a powerful tool in that both of these questions can be explored. While estradiol is the most potent estrogen, levels of estrone and estriol should also be considered when evaluating the patient's estrogen production. The other estrogen metabolites are better suited to answer questions about hydroxylation and methylation and not estrogen production. Ranges are based on mid-luteal (days 19-21) collections for females.

THE PATIENT REPORTS THE USE OF ORAL ESTROGENS. RESULTS MUST BE INTERPRETED CAREFULLY. IT IS LIKELY THAT SOME ESTROGEN METABOLITES (ESPECIALLY E1 AND E2) ARE ELEVATED. THIS DOES NOT NECESSARILY MEAN THERE IS TOO MUCH ESTROGEN. A LARGE FRACTION OF ESTROGENS INGESTED (LIKELY >50%) ARE METABOLIZED AND END UP IN URINE BEFORE ACTUALLY GETTING INTO CIRCULATION (1st-PASS METABOLISM). THIS IS UNIQUE TO ORAL EXPOSURE TO ESTROGENS, WHICH WHY SOME DO NOT FAVOR THIS ROUTE OF ADMINISTRATION (ALONG WITH THE FACT THAT ORAL ESTROGENS MAY INCREASE SEX HORMONE BINDING PROTEINS AND, TO SOME DEGREE, THE RISK OF BLOOD CLOTS AND STROKE). PATIENT SYMPTOMS ARE IMPORTANT IN GUIDING ANY NEEDED DOSING CHANGES. DOWNSTREAM METABOLITES OF E1 AND E2 MAY BE LESS IMPACTED BY 1st-PASS METABOLISM AND BETTER REFLECT ESTROGEN STATUS. ESTROGEN METABOLISM (HYDROXYLATION, METHYLATION) PATTERNS ARE IMPORTANT TO CONSIDER IN THESE CASES. A SIGNIFICANT AMOUNT OF ESTRONE IS CREATED WHEN ESTROGENS ARE DOSED ORALLY, SO ASSESSING HOW ESTRONE IS METABOLIZED IS IMPORTANT.

Estrogen Hydroxylation: Both estradiol and estrone can be hydroxylated by three competing enzymes. CYP 1A1 creates 2-OH-E1 and 2-OH-E2 (known for their protective effects), CYP 3A4 creates 16-OH-E1 and 16-OH-E2 (estriol), and CYP 1B1 creates the carcinogenic 4-OH-E1 and 4-OH-E2. These three competing pathways can be assessed with the pie chart shown on the report. If the patient shows less 2-OHE1 than expected, this can be increased with supplements like DIM and I3C or by consuming green, leafy vegetables that contain these compounds. These supplements may also decrease the most potent estrogens (estrone and estradiol) all of which can lead to a more favorable pattern with respect to risks of estrogen-mediated cancers.

2-OH and 4-OH Estrogen Methylation: Once hydroxylated estrogens have been formed, the 2 and 4-OH estrogens can be further metabolized. If they are successfully methylated, they can be excreted without causing harm. If they are not methylated, these reactive "catechol" estrogens can create quinone groups which can react with DNA building blocks (the purine blocks adenine and guanine more specifically) and create DNA-adducts. The 4-OH estrogens do this in a manner that is far more detrimental than 2-OH estrogens, which is why the 4-OH estrogens are considered carcinogens. 2-OH estrogens do make DNA-adducts but show an overall anti-estrogenic effect that may in fact be protective. The methylation efficiency is assessed by looking at the relationship between 2-OH-E1 and the corresponding 2-Methoxy-E1. 4-Methoxy-E1 is also reported, but these numbers tend to be very low, so this relationship is not considered in the methylation index. If the methylation of 4-OH-E1 tells a very different story than that of 2-OH-E1, this should be taken into consideration.

ADVANCED ADRENAL ASSESSMENT: When a physical or psychological stressor is introduced, the HPA-axis is prompted to produce ACTH which stimulates the adrenal gland to make cortisol and to a lesser extent DHEA and DHEA-S. In healthy individuals cortisol should rise rather rapidly in the first 10-30 minutes after waking and then decrease throughout the rest of the day, reaching a nadir in the middle of the night. Hyperactivity of the HPA-axis is seen in Cushing's Disease where cortisol is elevated all day. More moderate overactive cortisol production is seen in conditions such as depression. Conversely, very little cortisol is made in response to ACTH is Addison's disease and more modest deficiencies can be seen in a variety of situations where the adrenal gland is not appropriately responding to ACTH. It is also possible for patients to have cortisol deficiencies due to low levels of ACTH or CRH, but these are not common.

OVERALL FREE CORTISOL LEVELS ARE WITHIN THE EXPECTED RANGE. AS HIGH LEVELS OF STRESS WERE REPORTED BY THE PATIENT DURING PART OF THE TIME OF COLLECTION, THERE COULD BE SOME CONCERN THAT "NORMAL" LEVELS OF THE

STRESS HORMONES REPRESENT AN INADEQUATE ADRENAL RESPONSE TO STRESS.

Cortisol-Cortisone Shuttle: It is important not to think of the back-and-forth conversion of cortisol and cortisone as 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.

THE PATIENT'S THF/THE RATIO IMPLIES A MODEST PREFERENCE FOR CORTISOL (RELATIVE TO CORTISONE). THIS IS CONFIRMED BY THE FACT THAT THE RATIO OF FREE CORTISOL COMPARED TO FREE CORTISONE IS ALSO HIGH (COMPARED TO EXPECTED VALUES). THE PATIENT'S BMI IS HIGH AND THE PRESENCE OF CENTRAL ADIPOSITY MAY BE SOMEWHAT DUE TO THIS PREFERENCE FOR CORTISOL AND ALSO WILL EXACERBATE THE CORTISOL PREFERENCE AS 11b-HSD I ACTIVITY IS HIGH IN ADIPOSE TISSUE.

Cortisol Metabolism: While inter-conversion between cortisol and cortisone is reversible, their metabolism to THF and THE is not. This step happens primarily in the liver via 5a and 5b-reductase. When one or both of these enzymes is up-regulated (as seen with obesity, insulin resistance, and hyperthyroidism) an effective cortisol deficiency can occur even when a significant amount of cortisol is being produced by the adrenal glands. Without measuring these cortisol metabolites one cannot differentiate between cases where the adrenal glands truly do not produce adequate cortisol and those cases where low free cortisol is caused by hypermetabolism. These rates of metabolism are calculated by dividing the result for the cortisol metabolites (THE or aTHF+bTHF) by the daily total of free cortisol and cortisone.

BOTH CORTISOL AND CORTISONE ARE METABOLIZED AT HIGH RATES FOR THIS PATIENT. THIS PATTERN USUALLY IMPLIES LONG-TERM STRESS, WHICH UP-REGULATES THESE ENZYMES. INCREASED METABOLISM RATES ARE ALSO COMMONLY CAUSED BY OBESITY AND INSULIN RESISTANCE. IF THIS HYPERMETABOLISM WORSENS, IT MAY CREATE A SITUATION WHERE THERE IS A DEGREE OF CORTISOL DEFICIENCY EVEN THOUGH THE ADRENAL GLANDS ARE PRODUCING QUITE A LOT 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 SIGNIFICANTLY DISTURBED WITH LOW RESULTS IN THE MORNING AND ELEVATED LEVELS IN THE AFTERNOON/EVENING. THIS MAY BE CONTRIBUTING TO THE PATIENT'S REPORTED FATIGUE SYMPTOMS. HIGH LEVELS OF STRESS WERE REPORTED IN THIS TIME PERIOD, SO THE ELEVATED CORTISOL MAY BE DUE TO AN IMMEDIATE STRESSOR, AND THE CORTISOL PATTERN MAY BE LOW ALL DAY IN THE ABSENCE OF AN ACUTE STRESSOR. STRESS REDUCTION MAY HELP LOWER THE ELEVATED EVENING CORTISOL, AND ADRENAL SUPPORT MAY BE NEEDED TO ADDRESS THE LOW MORNING ADRENAL RESPONSE.

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 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 or blood collection, so it is technically considered "reseach only" for urine collection. Its proper use for urine collection has been thoroughly validated.