TEST REPORT

 # D2019 11 25 001 S

Ordering Provider:
Getuwell

Samples Received
11/25/2019

Report Date
11/26/2019

Samples Collected
Saliva - 11/21/19 07:20

Patient Name: LCMS Saliva PCOS
Patient Phone Number:

Gender Female	**Last Menses** Unspecified	**Height** 5 ft 5 in	**Waist** 40 in
DOB 11/6/1994 (25 yrs)	**Menses Status** Pre-Menopausal - Irregular	**Weight** 195 lb	**BMI** 32.4

TEST NAME	RESULTS | 11/21/19	RANGE
Salivary Steroids & Other Analytes (LC-MS/MS)		
Estradiol	3.2 H	1.0-2.9 pg/mL Premeno-luteal
Estriol	1	<3.0 pg/mL Premenopausal Luteal
Estrone	10.4 H	3.2-7.9 pg/mL Premeno-luteal
Ethinyl Estradiol	<0.4	<0.4 pg/mL
Pregnenolone Sulfate	10	1-23 pg/mL
Progesterone	60 L	66-196 pg/mL Premeno-luteal
Ratio: Pg/E2 (Saliva LCMS)	19 L	23-196
Allopregnanolone	<15.0	<15 pg/mL
17OH-Progesterone	45 H	6-28 pg/mL
Androstenedione	110 H	36-93 pg/mL
Testosterone	40 H	7-22 pg/mL
DHT	30 H	<25 pg/mL
DHEA	113	77-287 pg/mL
DHEAS	6.9	0.8-8.0 ng/mL
7-keto DHEA	100	41-130 pg/mL
11-Deoxycortisol	52 H	12-48 pg/mL
Cortisol	6.7 H	2.5-6.2 ng/mL Morning
Cortisone	20	10.0-23.3 ng/mL Morning

TEST NAME	RESULTS	11/21/19	RANGE
Salivary Steroids & Other Analytes (LC-MS/MS)		
Corticosterone	60	11-66 pg/mL
Aldosterone	65 H	16-63 pg/mL
Melatonin	17	3-22 pg/mL
Anastrozole	<5	<5 pg/mL
Finasteride	265	>5 pg/mL Finasteride
Letrozole	<5	<5 pg/mL

<dl = Less than the detectable limit of the lab. N/A = Not applicable; 1 or more values used in this calculation is less than the detectable limit. H = High. L = Low.

Therapies

2.5 mg oral Finasteride (Proscar, Propecia) (Pharmaceutical)

Saliva Steroid Cascade

Pregnenolone Sulfate

DHEA-S 7-Keto DHEA

11β-HSD1

ST | SU

ST | SU

Cholesterol CYPscc Pregnenolone 17-OH Pregnenolone 17, 20-Lyase DHEA TYPE 1 Androstenediol

3β-HSD

17α-OH

17β-HSD

TYPE 1

5α-R
3α-HSD

Allopregnanolone ← Progesterone 17-OH Progesterone → Androstenedione Testosterone

17, 20-Lyase

TYPE 2

21-OH

AR ⊣ ⊣ AR 5α-R ⊣ FIN

ANZ, LTZ

11-Deoxycorticosterone 11-Deoxycortisol

TYPE 1

Estrone ← Estradiol DHT

11β-OH

CYP3A4
17β-HSD

TYPE 2

Corticosterone Cortisol Estriol

AS

11β-HSD1 | 17β-HSD2

KEY
AR - Aromatase
AS - Aldosterone Synthase
ST - Sulfotransferase
SU - Sulfatase
Analytes in bold are reported by ZRT

Aldosterone Cortisone

Steroid Synthesis Inhibitors

Anastrozole
ANZ

Letrozole
LTZ

Finasteride
FIN

Synthetic Contraceptive Estrogen

Ethinyl Estradiol

Melatonin

Mel

Disclaimer: Symptom Categories below show percent of symptoms self-reported by the patient compared to total available symptoms for each category. For detailed information on category breakdowns, go to www.zrtlab.com/patient-symptoms.

SYMPTOM CATEGORIES — RESULTS | 11/21/19

Category	Result
Estrogen / Progesterone Deficiency	25%
Estrogen Dominance / Progesterone Deficiency	47%
Low Androgens (DHEA/Testosterone)	28%
High Androgens (DHEA/Testosterone)	69%
Low Cortisol	30%
High Cortisol	40%
Hypometabolism	23%
Metabolic Syndrome	76%

SYMPTOM CHECKLIST

(Scale: MILD — MODERATE — SEVERE)

Symptom	Severity
Aches and Pains	Mild
Acne	Moderate
ADD/ADHD	Minimal
Addictive Behaviors	Moderate
Allergies	Mild
Anxious	Moderate
Autism Spectrum Disorder	Minimal
Bleeding Changes	Minimal
Blood Pressure High	Moderate
Blood Pressure Low	Minimal
Blood Sugar Low	Minimal
Body Temperature Cold	Minimal
Bone Loss	Minimal
Breast Cancer	Minimal
Breasts - Fibrocystic	Mild
Breasts - Tender	Moderate
Chemical Sensitivity	Minimal
Cholesterol High	Severe
Constipation	Mild
Depressed	Moderate
Developmental Delays	Minimal
Eating Disorders	Severe
Fatigue - Evening	Mild
Fatigue - Morning	Moderate
Fibromyalgia	Minimal
Foggy Thinking	Minimal
Goiter	Minimal
Hair - Dry or Brittle	Minimal
Hair - Increased Facial or Body	Severe
Hair - Scalp Loss	Moderate
Headaches	Moderate
Hearing Loss	Minimal
Heart Palpitations	Mild
Hoarseness	Minimal
Hot Flashes	Minimal
Incontinence	Minimal
Infertility	Severe
Irritable	Moderate
Libido Decreased	Severe
Mania	Minimal

SYMPTOM CHECKLIST	MILD	MODERATE	SEVERE
Memory Lapse	███		
Mood Swings	████████████████████		
Muscle Size Decreased	█		
Nails Breaking or Brittle	█		
Nervous	██████████████		
Night Sweats	█		
Numbness - Feet or Hands	█		
OCD	█		
Panic Attacks	███████████		
PreMenstrual Dysphoric Disorder	BLANK		
Pulse Rate Slow	█		
Rapid Aging	█		
Rapid Heartbeat	█		
Skin Thinning	█		
Sleep Disturbed	███████████		
Stamina Decreased	████		
Stress	███████████████████		
Sugar Cravings	███████████		
Sweating Decreased	█		
Swelling or Puffy Eyes/Face	█		
Tearful	█		
Triglycerides Elevated	███████████		
Urinary Urge Increased	█		
Uterine Fibroids	█		
Vaginal Dryness	█		
Water Retention	███████████		
Weight Gain - Hips	███████████		
Weight Gain - Waist	██████████████████		

Lab Comments

Estradiol (E2) and estrone (E1) are higher than reference ranges for a premenopausal woman assuming that the saliva sample was collected during the luteal phase of the menstrual cycle (note: patient indicates irregular menstrual cycles). Symptoms are consistent with chronic high estrogens (estrogen dominance), which is usually associated low progesterone (Pg) relative to estradiol (i.e. low Pg/E2 ratio). For optimal effects of estradiol its level should be within mid-luteal ranges (about 1.5-3 pg/ml) and well balanced with progesterone, optimally with a Pg/E2 ratio of about 100-500. Consider means to lower the high estradiol with diet (more fiber, colored vegetables, less red meat, fewer empty carbohydrates), exercise, stress reduction, and natural progesterone. Progesterone helps regulate estradiol by increasing the levels and activity of enzymes that convert it to less active estrone and then to inert estrone sulfate. Progesterone at high physiological concentrations seen during the luteal phase of the menstrual cycle (10-30 mg), or used as progesterone therapy also down-regulate cellular estrogen receptors in target tissues such as the breasts and uterus, preventing estradiol from stimulating further cell hypertrophy and proliferation that occur during mid follicular phase/ ovulation, and in women approaching menopause with excessive estradiol synthesis and luteal insufficiency (low progesterone).

Progesterone (Pg) is lower than luteal range and is not well balanced with estradiol (low Pg/E2). Low Pg is consistent with symptoms of estrogen dominance. The downstream Pg metabolite allopregnanolone (AlloP) is very low (less than detectable range). AlloP is a potent neuroactive steroid in the brain that amplifies the anxiolytic (calming) actions of GABA on the GABAergic neurons, which helps balance the anxiogenic (stimulating) actions of excessive levels of estrogens. Allopregnanolone is created from progesterone through the actions of 5-alpha reductase (5aR) and 3-alpha hydroxysteroid dehydrogenase (3aHSD), which convert Pg to 5-hydroxyprogesterone (5OHPg) and then to AlloP. This individual reports use of Finasteride, a potent synthetic inhibitor of 5aR that blocks conversion of T to DHT, and Pg to 5OHP, a precursor to AlloP. Very low AlloP is likely the result of Finasteride therapy to suppress symptoms of androgen excess, as self-reported. While Finasteride has been shown to be effective for treating hair loss and hirsutism caused by high testosterone/DHT, it can cause adverse side effects such as anxiety and depression, symptoms commonly associated with low AlloP.

Testosterone (T), is higher than reference range for a premenopausal woman. Precursors for testosterone, 17-hydroxyprogesterone (17OHP) and androstenedione (Adione) are also higher than range. However, dihydrotestosterone (DHT), the downstream metabolite of T and responsible for many of the final actions of androgens at the cellular level, is lower than detectable range, indicating low 5 alpha reductase (5aR) activity. This individual indicates recent use of Finasteride, a 5aR inhibitor often used by women with PCOS and symptoms of androgen excess such as scalp hair loss, acne, and excessive facial/body hair. By inhibiting 5aR this often results in accumulation of hormones upstream of the inhibitor, which would include T, Adione, and 17OHP. High levels of these hormones in combination with high estrogens, low progesterone,

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irregular menstrual cycles, and symptoms of androgen excess (e.g. loss of scalp hair, increased facial/body hair, and/or acne) strongly suggest Polycystic Ovarian Syndrome (PCOS), a condition found to occur in approximately 8-10% of premenopausal women. PCOS is closely associated with excessive weight gain, poor diet consisting of excessive carbohydrate consumption, and insulin resistance. Various natural and synthetic inhibitors are used to lower the androgenic burden by inhibiting T synthesis (synthetic progestins, LH antagonists) or DHT synthesis by inhibition of 5aR (Finasteride, Saw Palmetto, natural progesterone). While all are effective for reducing DHT, if inhibition is excessive it could lead to very low levels of DHT's downstream metabolite 3a5a-androstanediol (Adiol), a neuroactive steroid with beneficial actions on the gabaergic and dopaminergic receptors in the brain. Low Adiol may exacerbate symptoms associated with low dopamine, which include food craving, low stamina, lack of focus, moodiness, forgetfulness, fatigue, apathy, and feelings of depression and sadness. If these adverse symptoms have become more problematic with use of Finasteride consider reducing dosage or consider other more natural means to block excessive formation of DHT (e.g. natural progesterone, treatment for insulin resistance if problematic).

The adrenal androgen precursors DHEA, DHEA-sulfate (DHEA-S), and 7-keto DHEA are within reference ranges for a premenopausal female. DHEA and 7-Keto DHEA are present in saliva in approximately equal amounts. Supplementation with DHEA raises levels of DHEA and downstream metabolites such as androstenedione, testosterone, and estrogens estrone and estradiol. In contrast, 7-keto DHEA, while it has beneficial anabolic effects and amplifies the actions of thyroid hormones, does not metabolize to downstream androgens or estrogens, like DHEA. Supplementation with 7-keto DHEA raises only its levels in saliva, resulting in a very high 7-keto DHEA/DHEA ratio. Supplementation with DHEA results in a very high DHEA/7-keto DHEA ratio and is useful for identifying individuals that may knowingly or unknowingly be using supplements that contain DHEA.

Cortisol is slightly elevated and its upstream precursors 11-deoxycortisol and 17-OH progesterone are also within the upper quadrant and higher than the reference ranges, respectively. Higher levels of these adrenal cortisol precursors and cortisol, in combination with high androgens are a hallmark of PCOS. Elevated cortisol is associated with insulin resistance, high insulin and hyperglycemia, and the etiology of PCOS. Stress reduction, removal of inflammatory foods, and natural progesterone can help counter the negative effects of chronic high cortisol. High cortisol likely contributes to self-reported sleep disturbances.

Aldosterone and its precursor corticosterone are higher than reference ranges, consistent with self-reported high blood pressure. Aldosterone is produced in the outer most zone of the adrenal gland. It regulates the body's levels of sodium and potassium through its actions on the kidney to increase sodium reabsorption and increase potassium excretion. High aldosterone (hyperaldosteronism) occurs frequently in women with PCOS and insulin resistance. High aldosterone is correlated directly with higher C-reactive protein, thickening of the intima-media of the carotid artery, lower HDL-cholesterol, and lower serum potassium, all of which increase lifetime risk for cardiovascular disease. Natural therapies to treat insulin resistance (weight control, diet, exercise, stress reduction, etc.), or synthetic drugs (e.g. Spironolactone, calcium channel blockers) to treat the more immediate deleterious effects of high aldosterone and low potassium should be discussed with a health care practitioner.

Melatonin in the first morning saliva sample is within expected reference range. This test only measures the first morning saliva, which if collected on awakening should be within reference range, as is not meant to evaluate melatonin at night before bed. However, if early nighttime melatonin is low this may aggravate being able to fall asleep. Melatonin is an antioxidant and supplementation may help with better sleep patterns and help lower cortisol, which at high levels contributes to insulin resistance.