NutriPATH
Integrative Pathology Services
P: 1300 688 522
E: info@nutripath.com.au
A: PO Box 442 Ashburton VIC 3142

TEST PATIENT
Sample Test Name
Sex : F
Date Collected : 00-00-0000
111 TEST ROAD TEST SUBURB
LAB ID: 00000000 UR#:0000000

TEST PHYSICIAN
DR JOHN DOE
111 CLINIC STREET
CLINIC SUBURB VIC 3000

Samples Arrived: 19/10/2015
Date Closed: 24/10/2015

Samples Collected: Urine: 18/10/2015 07:50
Urine 18/10/2015 10:10
Urine: 18/10/2015 17:05
Urine: 18/10/2015 20:45

BMI: 23.5
Height: 169 cm
Weight: 67 kg
Waist: 75 cm

Menses Status: Pre-Menopausal - Irregular
Gender: Female

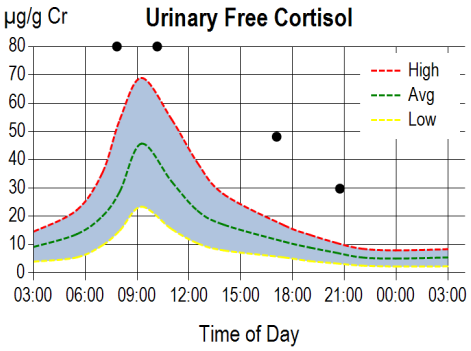
Last Menses: 26/07/2014
DOB: (26 yrs) Patient Ph#: 0000000000

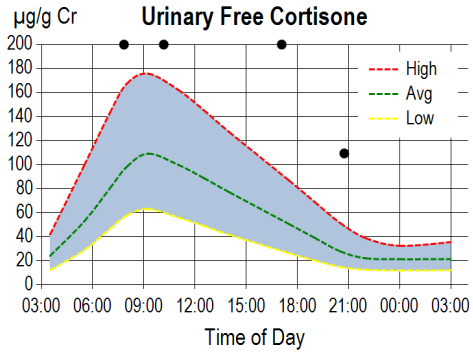
Test Name	Result		Range
Urinary Estrogens (µg/g Cr)			
Estradiol (Urine)	0.17	L	0.78-1.79 Premeno-luteal or ERT
Estrone (Urine)	0.47	L	2.27-5.22 Premeno-luteal or ERT
Estriol (Urine)	0.55	L	0.78-1.98 Premeno-luteal or ERT
E3/(E1+E2) (Urine)	0.86		>0.3 (> median value)
2-OH Estradiol (Urine)	0.10	L	0.17-0.70 Premeno-luteal or ERT
2-OH Estrone (Urine)	0.28	L	0.70-2.54 Premeno-luteal or ERT
4-OH Estradiol (Urine)	0.14		0.10-0.18 Premeno-luteal or ERT
4-OH Estrone (Urine)	0.09	L	0.17-0.47 Premeno-luteal or ERT
16α-OH Estrone (Urine)	0.21	L	0.35-1.07 Premeno-luteal or ERT
2-OH (E1 + E2)/16-α-OH E1 (Urine)	1.81		1.29-5.49 Premeno-luteal or ERT
2-MeO Estradiol (Urine)	0.05		0.03-0.08 Premeno-luteal or ERT
2-MeO Estrone (Urine)	0.08	L	0.26-0.68 Premeno-luteal or ERT
2-MeO E1/2-OH E1 (Urine)	0.29		0.21-0.38 Premeno-luteal or ERT
4-MeO Estradiol (Urine)	<0.04		< 0.04
4-MeO Estrone (Urine)	0.04		< 0.04
4-MeO E1/4-OH E1 (Urine)	0.44	H	0.05-0.13 Premeno-luteal or ERT
4-MeO E2/4-OH E2 (Urine)	0.14		0.10-0.29 Premeno-luteal or ERT
Urinary Progestogens (µg/g Cr)			
Pregnanediol (Urine)	203	L	465-1609 Premeno-luteal or PgRT
Pgdiol/E2 (Urine)	1194.12		1000-1500 (Optimal Luteal Only)
Allopregnanolone (Urine)	1.12	L	2.23-14.87 Premeno-luteal or PgRT
Allopregnanediol (Urine)	4.75	L	14.65-76.71 Premeno-luteal or PgRT
3α-Dihydroprogesterone (Urine)	1.07		0.67-2.03 Premeno-luteal or PgRT
20α-Dihydroprogesterone (Urine)	6.87		3.93-11.62 Premeno-luteal or PgRT
Deoxycorticosterone (Urine)	0.42	L	0.69-2.23 Premeno-luteal or PgRT
Corticosterone (Urine)	8.63		3.19-9.59 Premeno-luteal or PgRT
Urinary Androgens (µg/g Cr)			
Testosterone (Urine)	3.84		1.22-3.97 Premeno-luteal or ART
Epi-Testosterone (Urine)	1.27	L	2.01-4.66 Premeno-luteal
T/Epi-T (Urine)	3.02	H	0.5-3.0
5α-DHT (Urine)	0.98		0.28-1.52 Premeno-luteal or ART
Androstenedione (Urine)	13.93	H	3.93-13.53 Premeno-luteal or ART

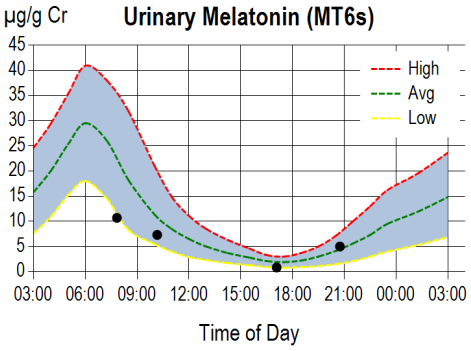
Test Name	Result		Range
DHEA (Urine)	137.22	H	15.82-129.17 Premeno-luteal or DHEAT
Urinary Glucocorticoids (µg/g Cr)			
Total Cortisol (Urine)	41.52	H	12.26-33.12 Premeno-luteal
Total Cortisone (Urine)	102.59	H	23.27-50.88 Premeno-luteal
Cortisol/Cortisone (Urine)	0.40	L	0.5-0.7
Tetrahydrocortisol (Urine)	455		214-546 Premeno-luteal
Tetrahydrocortisone (Urine)	1333	H	437-1184 Premeno-luteal
Urinary Free Diurnal Cortisol (µg/g Cr)			
Free Cortisol (Urine)	143.84	H	7.8-29.5 (1st Morning)
Free Cortisol (Urine)	116.50	H	23.4-68.9 (2nd Morning)
Free Cortisol (Urine)	48.12	H	6.0-19.2 (Evening)
Free Cortisol (Urine)	29.79	H	2.6-8.4 (Night)
Urinary Free Diurnal Cortisone (µg/g Cr)			
Free Cortisone (Urine)	774.71	H	31.6-91.6 (1st Morning)
Free Cortisone (Urine)	420.02	H	63.3-175.8 (2nd Morning)
Free Cortisone (Urine)	290.31	H	30.6-88.5 (Evening)
Free Cortisone (Urine)	109.49	H	15.5-44.7 (Night)
Urinary Diurnal Melatonin MT6s (µg/g Cr)			
Melatonin (Urine)	10.69	L	18.0 - 40.9 (1st Morning)
Melatonin (Urine)	7.30		7.3 - 31.9 (2nd Morning)
Melatonin (Urine)	0.83		0.7 - 2.2 (Evening)
Melatonin (Urine)	4.99		1.7 - 11.1 (Night)
Urinary Creatinine (mg/mL)			
Creatinine (pooled) (Urine)	0.23	L	0.3-2.0
Creatinine (Urine)	0.29	L	0.3-2.0 (1st morning)
Creatinine (Urine)	0.14	L	0.3-2.0 (2nd morning)
Creatinine (Urine)	0.12	L	0.3-2.0 (Evening)
Creatinine (Urine)	0.15	L	0.3-2.0 (Night)

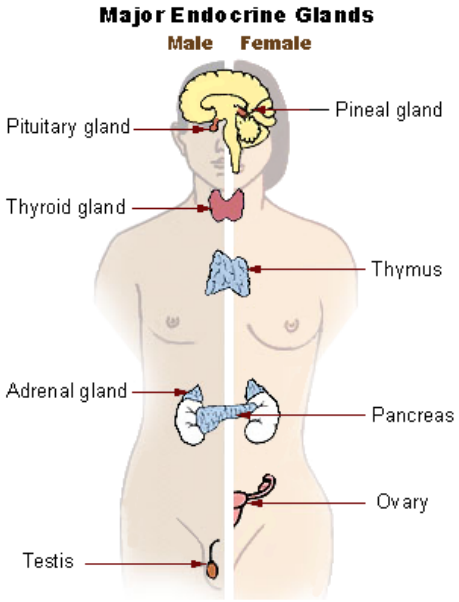
Therapies

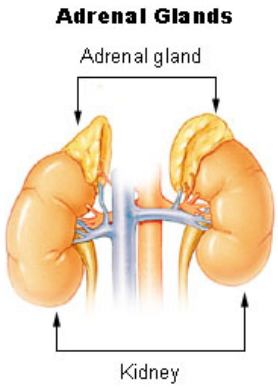
None Indicated











Laboratory Reference Ranges

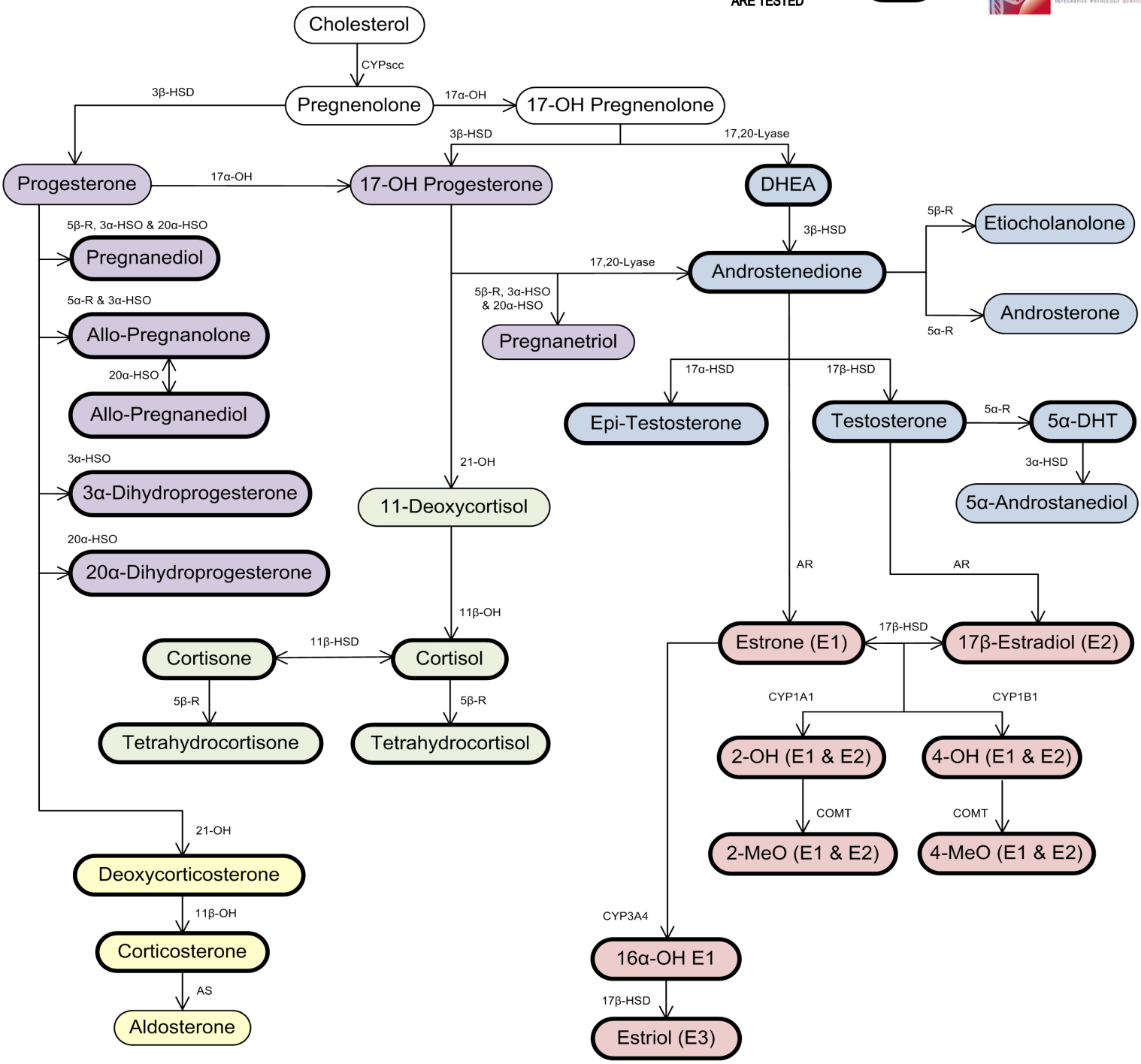
Disclaimer: Supplement type and dosage are for informational purposes only and are not recommendations for treatment.

Test Name	Women
Estradiol (Urine) - µg/g Cr	0.13-0.78 Postmenopausal; 0.78-1.96 Premeno-luteal or ERT; 0.15-0.75 Postmenopausal; 0.78-1.79 Premeno-luteal or ERT
Estrone (Urine) - µg/g Cr	0.59-2.70 Postmenopausal; 2.37-5.48 Premeno-luteal or ERT; 0.64-2.56 Postmenopausal; 2.27-5.22 Premeno-luteal or ERT
Estriol (Urine) - µg/g Cr	0.25-1.15 Postmenopausal; 0.76-2.13 Premeno-luteal or ERT; 0.28-1.17 Postmenopausal; 0.78-1.98 Premeno-luteal or ERT
E3/(E1+E2) (Urine) - µg/g Cr	>0.3 (> median value)
2-OH Estradiol (Urine) - µg/g Cr	0.07-0.30 Postmenopausal; 0.15-0.82 Premeno-luteal or ERT; 0.08-0.31 Postmenopausal; 0.17-0.70 Premeno-luteal or ERT
2-OH Estrone (Urine) - µg/g Cr	0.21-1.11Postmenopausal; 0.81-2.90 Premeno-luteal or ERT; 0.25-1.00 Postmenopausal; 0.70-2.54 Premeno-luteal or ERT
4-OH Estradiol (Urine) - µg/g Cr	0.03-0.11 Postmenopausal; 0.11-0.24 Premeno-luteal or ERT; 0.03-0.12 Postmenopausal; 0.10-0.18 Premeno-luteal or ERT
4-OH Estrone (Urine) - µg/g Cr	0.05-0.23 Postmenopausal; 0.17-0.49 Premeno-luteal or ERT; 0.06-0.22 Postmenopausal; 0.17-0.47 Premeno-luteal or ERT
16α-OH Estrone (Urine) - µg/g Cr	0.08-0.42 Postmenopausal; 0.31-1.02 Premeno-luteal or ERT; 0.10-0.41 Postmenopausal; 0.35-1.07 Premeno-luteal or ERT
2-OH (E1 + E2)/16-α-OH E1 (Urine) - µg/g Cr	1.47-8.17 Postmenopausal; 1.77-13.42 Postmenopausal; 1.29-5.49 Premeno-luteal or ERT; 1.81-5.21 Premeno-luteal or ERT
2-MeO Estradiol (Urine) - µg/g Cr	0.02-0.05 Postmenopausal; 0.03-0.09 Premeno-luteal or ERT; 0.02-0.07 Postmenopausal; 0.03-0.08 Premeno-luteal or ERT
2-MeO Estrone (Urine) - µg/g Cr	0.06-0.27 Postmenopausal; 0.25-0.71 Premeno-luteal or ERT; 0.06-0.29 Postmenopausal; 0.26-0.68 Premeno-luteal or ERT
2-MeO E1/2-OH E1 (Urine) - µg/g Cr	0.19-0.36 Postmenopausal; 0.21-0.38 Premeno-luteal or ERT
4-MeO Estradiol (Urine) - µg/g Cr	0.01-0.04 Postmenopausal; 0.02-0.04 Premeno-luteal or ERT; < 0.04
4-MeO Estrone (Urine) - µg/g Cr	0.01-0.03 Postmenopausal; 0.01-0.03 Premeno-luteal or ERT; < 0.04
4-MeO E1/4-OH E1 (Urine) - µg/g Cr	0.03-0.38 Postmenopausal; 0.05-0.13 Premeno-luteal or ERT
4-MeO E2/4-OH E2 (Urine) - µg/g Cr	0.14-0.73 Postmenopausal; 0.10-0.29 Premeno-luteal or ERT
Pregnanediol (Urine) - µg/g Cr	43-168 Postmenopausal; 579-1710 Premeno-luteal or PgRT; 56-220 Postmenopausal; 465-1609 Premeno-luteal or PgRT
Pgdiol/E2 (Urine) - µg/g Cr	1000-1500 (Optimal Luteal Only)
Allopregnanolone (Urine) - µg/g Cr	0.22-1.08 Postmenopausal; 2.81-16.36 Premeno-luteal or PgRT; 0.3-1.31 Postmenopausal; 2.23-14.87 Premeno-luteal or PgRT
Allopregnanediol (Urine) - µg/g Cr	0.82-4.16 Postmenopausal; 16.64-72.85 Premeno-luteal or PgRT; 1.38-6.75 Postmenopausal; 14.65-76.71 Premeno-luteal or PgRT
3α-Dihydroprogesterone (Urine) - µg/g Cr	0.13-0.56 Postmenopausal; 0.77-1.91 Premeno-luteal or PgRT; 0.19-0.77 Postmenopausal; 0.67-2.03 Premeno-luteal or PgRT
20α-Dihydroprogesterone (Urine) - µg/g Cr	0.49-2.21 Postmenopausal; 3.09-9.30 Premeno-luteal or PgRT; 0.60-5.53 Postmenopausal; 3.93-11.62 Premeno-luteal or PgRT
Deoxycorticosterone (Urine) - µg/g Cr	0.32-1.45 Postmenopausal; 0.63-1.52 Premeno-luteal or PgRT; 0.37-1.97 Postmenopausal; 0.69-2.23 Premeno-luteal or PgRT
Corticosterone (Urine) - µg/g Cr	1.58-6.75 Postmenopausal; 3.27-7.88 Premeno-luteal or PgRT; 2.32-9.88 Postmenopausal; 3.19-9.59 Premeno-luteal or PgRT
Testosterone (Urine) - µg/g Cr	0.55-2.34 Postmenopausal; 0.71-3.75 Premeno-luteal or ART; 0.66-2.89 Postmenopausal; 1.22-3.97 Premeno-luteal or ART

Test Name	Women
Epi-Testosterone (Urine) - µg/g Cr	0.30-0.90 Postmenopausal; 2.21-5.12 Premeno-luteal; 0.39-1.32 Postmenopausal; 2.01-4.66 Premeno-luteal
T/Epi-T (Urine) - µg/g Cr	0.5-3.0
5α-DHT (Urine) - µg/g Cr	0.18-0.72 Postmenopausal; 0.20-1.29 Premeno-luteal or ART; 0.26-0.98 Postmenopausal; 0.28-1.52 Premeno-luteal or ART
Androstenedione (Urine) - µg/g Cr	1.98-4.75 Postmenopausal; 3.75-11.55 Premeno-luteal or ART; 2.07-7.94 Postmenopausal; 3.93-13.53 Premeno-luteal or ART
DHEA (Urine) - µg/g Cr	7.85-28.80 Postmenopausal; 16.90-54.67 Premeno or DHEAT; 8.63-37.28 Postmenopausal; 15.82-129.17 Premeno-luteal or DHEAT
Total Cortisol (Urine) - µg/g Cr	10.22-23.92 Postmenopausal; 11.83-31.10 Premenopausal; 13.23-39.26 Postmenopausal; 12.26-33.12 Premeno-luteal
Total Cortisone (Urine) - µg/g Cr	18.80-39.46 Postmenopausal; 23.70-48.92 Premenopausal; 23.32-59.61 Postmenopausal; 23.27-50.88 Premeno-luteal
Cortisol/Cortisone (Urine) - µg/g Cr	0.5-0.7
Tetrahydrocortisol (Urine) - µg/g Cr	232-518 Postmenopausal; 254-733 Premenopausal; 281-711 Postmenopausal; 214-546 Premeno-luteal
Tetrahydrocortisone (Urine) - µg/g Cr	421-1043 Postmenopausal; 421-1240 Premenopausal; 551-1474 Postmenopausal; 437-1184 Premeno-luteal
Free Cortisol (Urine) - µg/g Cr	8.5 - 30.5 (1st Morning); 7.8-29.5 (1st Morning); 23.4-68.9 (2nd Morning); 20.7 - 56.9 (2nd Morning); 7.1 - 17.5 (Evening); 6.0-19.2 (Evening); 2.6-8.4 (Night); 3.1 - 9.0 (Night)
Free Cortisone (Urine) - µg/g Cr	31.6-91.6 (1st Morning); 33.5 - 93.9 (1st Morning); 63.3-175.8 (2nd Morning); 58.8 - 140 (2nd Morning); 30.6-88.5 (Evening); 36.9 - 82.1 (Evening); 15.5-44.7 (Night); 18.4 - 47.7 (Night)
Melatonin (Urine) - µg/g Cr	18.0 - 40.9 (1st Morning); 7.3 - 31.9 (2nd Morning); 0.7 - 2.2 (Evening); 1.7 - 11.1 (Night)
Creatinine (pooled) (Urine) - mg/mL	0.3-2.0; 0.3-3.0
Creatinine (Urine) - mg/mL	0.3-3.0 (1st Morning); 0.3-3.0 (2nd Morning); 0.3-3.0 (Evening); 0.3-3.0 (Night); 0.3-2.0 (1st morning); 0.3-2.0 (2nd morning); 0.3-2.0 (Evening); 0.3-2.0 (Night)

The Steroid Hormone Cascade

Metabolites in **Bold** ARE TESTED



Androgens

Estrogens

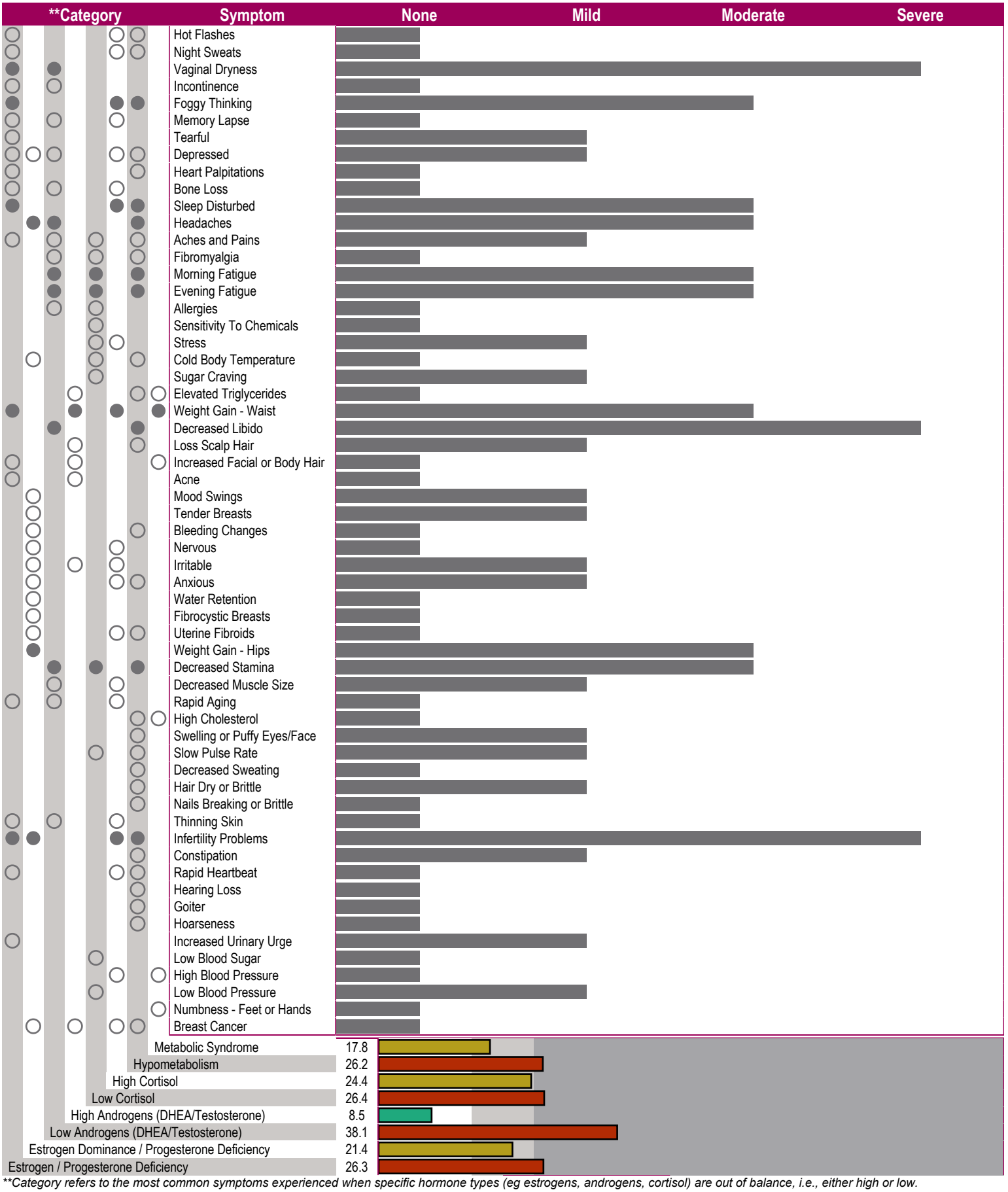
Glucocorticoids

Mineralocorticoids

Progestogens

Enzyme Abbreviations

(3α-HSO) 3α-Hydroxysteroid oxidoreductase
(20α-HSO) 20α-Hydroxysteroid oxidoreductase
(5α-R) 5α-Reductase
(5β-R) 5β-Reductase
(11β-OH) 11β-Hydroxylase
(17α-OH) 17α-Hydroxylase
(21-OH) 21-Hydroxylase
(3α-HSD) 3α-Hydroxysteroid dehydrogenase
(3β-HSD) 3β-Hydroxysteroid dehydrogenase
(11β-HSD) 11β-Hydroxysteroid dehydrogenase
(17α-HSD) 17α-Hydroxysteroid dehydrogenase
(17β-HSD) 17β-Hydroxysteroid dehydrogenase
(AR) Aromatase
(AS) Aldosterone Synthase
(CYP) Cytochrome p450 (scc, 1A1, 1B1 & 3A4)
(COMT) Catechol-O-Methyl-Transferase



***Category refers to the most common symptoms experienced when specific hormone types (eg estrogens, androgens, cortisol) are out of balance, i.e., either high or low.*

Lab Comments

Estrogens (estradiol, estrone, estriol) and their down-stream catechol metabolites and methylated catechols are low. Because androgens (testosterone, androstenedione, DHEA) as estrogen precursors are within high-normal reference ranges this suggests low aromatase activity, which may contribute to self-reported infertility and symptoms of estrogen deficiency.

PROGESTERONE METABOLITES (PREGNANEDIOL)

Pregnanediol is lower than the expected reference range for a premenopausal woman, assuming the sample was collected during the luteal phase of the menstrual cycle (not likely as patient has not had a menstrual cycle in over one year, and self-reports intertility.. Pregnanediol is a metabolite of progesterone that is excreted into urine. Levels of pregnanediol closely parallel those of progesterone in serum, making pregnanediol a good surrogate marker of circulating levels of progesterone.

Low pregnanediol, assuming urine was collected during peak luteal phase of the menstrual cycle (about days 19-21 of a 28 day cycle with day 1 the first day of menses), usually indicates luteal insufficiency. This is a condition where ovulation occurs (egg is released from the ovaries) but is not followed by sufficient progesterone to maintain a pregnancy, should it occur. Luteal insufficiency is common in the latter years of premenopause, often referred to as perimenopause.

Low pregnanediol might also occur as a result of anovulation, which can result from very low production of the sex-hormones (estrogens, progesterone, and testosterone) or from a condition referred to as Poly Cystic Ovarian Syndrome (PCOS), which is associated with irregular menstrual cycles, normal to high estrogens (estradiol and estrone), low progesterone, high testosterone, and a high ratio of LH to FSH. PCOS is thought to be caused by insulin resistance, which is linked to metabolic syndrome (obesity, elevated blood lipids, high blood pressure) and increased lifetime risk for cardiovascular disease, strokes, and cancer.

Progesterone therapy is often helpful when estradiol levels are normal to elevated, urinary pregnanediol is low, and symptoms of estrogen imbalance (both estrogen deficiency and dominance) are problematic.

PROGESTERONE METABOLITES (PREGNANES AND PREGNENES)

The pregnane (allopregnanolone and allopregnanediol) categories of progesterone metabolites are low, or lower than the median, of the expected reference ranges for a premenopausal woman, whereas the pregnene category of metabolites (3-alpha-dihydroxyprogesterone and 20-alpha-dihydroprogesterone) are within normal range. This indicates that progesterone is not converting to the pregnane category of down-stream progesterone metabolites, which is likely due to a low 5-alpha-reductase (same enzyme that converts testosterone to the more potent dihydrotestosterone.

One of the pregnane metabolites of progesterone is allopregnanolone, which is well studied and a known anxiolytic neurosteroid that binds to brain GABA receptors, resulting in a calming and sleep-inducing effect. Higher levels of this progesterone metabolite are associated with a lower incidence of PMS in premenopausal women and better sleep patterns in both premenopausal women with normal menstrual cycles and postmenopausal women supplementing with exogenous progesterone.

In some individuals who convert large amounts of progesterone (endogenous during pregnancy or exogenous from supplementation, mostly oral) to allopregnanolone, the sleep-inducing effect can be overwhelming. If exogenous progesterone supplementation causes excessive drowsiness, you are likely a high pregnane metabolizer, and it is best to use it only before bed. If the low allopregnanolone, as reported herein, is associated with sleep disturbances, it may be worthwhile to consider oral progesterone, as this usually results in higher production of this anxiolytic progesterone metabolite.

MINERALCORTICOID PRECURSORS

Deoxycorticosterone (DOC) is lower than the median reference range for a premenopausal woman. In contrast, corticosterone (CC) is within the high-normal range. Low DOC and elevated CC suggests high levels of the enzyme 11-beta HSD (converts DOC to CC and 11-deoxycortisol to cortisol (note: total cortisol and tetrahydrocortisol, a down-stream metabolite of cortisol, are also elevated). Lower DOC and higher CC is thought to be caused by a metabolic defect in aldosterone synthesis from corticosterone, which leads to accumulation of CC, low aldosterone, and associated symptoms of hypoaldosteronism (low blood pressure and faintness with standing up, frequent urination, salt wasting, hearing problems, fatigue, poor exercise tolerance and painful muscles and joints). Cortisol and down stream metabolites are usually within normal range with this defect in aldosterone synthesis.

ANDROGEN PRECURSORS (ANDROSTENEDIOL, DHEA)

DHEA(S) and androstenedione are slightly higher than reference ranges for a premenopausal woman.

Androstenedione is the precursor to testosterone, which in the presence of aromatase is converted to estradiol, and in the presence of 5-alpha reductase is converted to the more potent androgen, dihydrotestosterone. In premenopausal women about half of the androstenedione is derived from the ovaries and the other half from the adrenals. At menopause, most of the androstenedione derives from the adrenal glands. DHEA is synthesized in the adrenal glands and is rapidly sulfated to DHEA-sulfate (DHEAS) to extend its half-life in blood.

High androgens are often associated with androgen excess symptoms. Paradoxically, many of the symptoms self-reported are more characteriistic of LOW androgens, which suggests that these symptoms are more likely due to other hormonal imbalances (e.g. high cortisol or low thyroid).

ANDROGENS AND METABOLITES (TESTOSTERONE, EPI-TESTOSTERONE, AND 5-ALPHA-DIHYDROTESTOSTERONE)

Testosterone (T) and DHT are within the reference ranges for a premenopausal woman.

Epi-testosterone (Epi-T) is lower than the reference range, resulting in a low T/Epi-T ratio. Epi-T and T are synthesized endogenously in about equal amounts from androstenedione, a down-stream metabolite of DHEA. With endogenous production the T/Epi-T ratio is about 1, and ranges from about 0.5-2. When testosterone is supplemented the T rises in proportion to dosage, but Epi-T remains the same, reflecting endogenous production.

Physiological levels of androgens (T and DHT) are important for strengthening structural tissues such as muscles, bone, connective tissue, and skin. They also play an important role in the brain to increase the level of neurotransmitters such as dopamine, which are important for mood elevation and sex drive. T is also a precursor to estradiol via the enzyme aromatase. Recent studies have shown that testosterone and DHT have a protective effect as regards breast cancer risk (Glaser RL, Maturitas 76: 342-349, 2013).

TOTAL GLUCOCORTICOIDS (Cortisol-F, Cortisone-E)

Total cortisol (F) and cortisone (E) are higher than the expected reference ranges for a premenopausal woman. The total levels of these glucocorticoids are determined from the average of four urine collections throughout the day and are very similar to the 24 hour urine values.

An acute high cortisol is a normal and healthy response to a stressor; however a chronically high cortisol caused by a persistent stressor can lead to multiple dysfunctions and disease. Elevated cortisol is usually caused by different types of stressors (emotional, physical-(e.g. excessive exercise, injury, surgery), chemical-(e.g. environmental pollutants, medications), inflammations-(e.g. cancer, metabolic syndrome), pathogens-(e.g. bacterial, fungal, viral infections). Typical acute symptoms/signs of high cortisol can include anxiety, nervous-irritability, self-perceived stress, sleep disturbances. More chronic elevated cortisol is commonly associated with the same symptoms seen with acutely high cortisol but also include memory problems, depression, loss of muscle mass, and weight gain in the waist. Immune suppression caused by chronic high cortisol can increase risk for cancer. Insulin resistance and metabolic syndrome are also a consequence and cause of elevated cortisol, as are the diseases of aging such as diabetes, cardiovascular disease, cancer, and bone loss. When cortisol remains high these symptoms/conditions/syndromes/diseases progressively become more problematic over time.

Evaluation of the diurnal pattern of cortisol (see below) is important as high night cortisol is more detrimental than high cortisol levels during the day and following a normal circadian rhythm (see Urinary Free Cortisol). For additional information about strategies for supporting adrenal health and reducing stress(ors), the following books are worth reading: "Adrenal Fatigue", by James L. Wilson, N.D., D.C., Ph.D.; "The Cortisol Connection", by Shawn Talbott, Ph.D.; "The End of Stress As We Know It" by Bruce McEwen; "Awakening Athena" by Kenna Stephenson, MD.

URINARY FREE CORTISOL (UFC)

The Urinary Free Cortisols, as well as cortisone, the down-stream inert metabolite of cortisol, are following a normal circadian rhythm but are higher than the normal reference ranges throughout the day.

Chronic high cortisol, particularly at night, leads to conditions such as weight gain in the waist, muscle and bone loss, depression, and immune suppression (note: night cortisol is low). Dysfunction of other hormones is closely associated with chronic excess cortisol. For example, tissue resistance to insulin, caused by chronically high cortisol, leads to insulin resistance/metabolic syndrome (expect to see symptoms characteristic of metabolic syndrome such as high blood pressure, elevated blood lipids). A persistently high night cortisol can eventually lower melatonin production, which is important for maintaining normal biorhythms and immune function. Because chronic stressors and associated high night cortisol can have adverse effects on health and wellbeing, it is important to develop strategies to identify and eliminate or reduce the stressors or consider bioidentical hormone

replacement therapies, foods, and/or nutritional supplements that help control excessive accumulation of cortisol. For additional information about adrenal dysfunction and strategies for adrenal support and lowering stress/cortisol levels the following books and journal articles are worth reading: "Adrenal Fatigue," by James L. Wilson, N.D., D.C., Ph.D.; "The Cortisol Connection," by Shawn Talbott, Ph.D.; "The End of Stress As We Know It," by Bruce McEwen.

MELATONIN METABOLITE 6-SULFATOXYMELATONIN (MT6s)

The melatonin metabolite MT6s is low to low-normal (flat pattern) throughout most of the day, and not showing a normal circadian rhythm. Low melatonin can contribute to self-reported sleep problems. If melatonin supplementation is not helpful for sleep issues, consider that other hormonal imbalances may be responsible.

When melatonin is within normal range but sleep issues are problematic, this condition may, more likely, be related to excessive stress(ors) or to other hormonal imbalances (low or high) in estrogens (necessary for REM sleep, excessive levels can be over stimulating), progesterone (metabolite allopregnanolone binds GABA receptors and has a calming effect), cortisol (low or high levels can disrupt sleep) and/or thyroid. If any of the symptoms of estrogen, progesterone, cortisol, or thyroid hormones appear to be imbalanced, consider testing them and correcting imbalances to facilitate better sleep.

In a healthy individual the circadian rhythm of melatonin is inversely related to cortisol, i.e. melatonin levels in blood, urine, and saliva rise with darkness and peak about 2-3 am, while cortisol falls to a nadir at this time of day. With morning and onset of light exposure, melatonin drops rapidly and cortisol begins to rise, peaking about 30 min to 1 hr after waking and exposure to light. By mid-afternoon melatonin reaches a nadir and then gradually begins to rise again with nightfall and less light exposure. Cortisol continues to fall as melatonin rises again, when both hormones reach their nadir and peak, respectively, about 2-3 am. Melatonin synthesis by the pineal gland is controlled by light exposure, while cortisol synthesis is controlled by the hypothalamic-pituitary axis in response to stressors.

Melatonin is known to have many different beneficial effects in the body. It helps slow the aging process, is a potent anti-oxidant, inhibits formation and growth of tumors such as breast and prostate cancers, and helps regulate the synthesis of the sex-hormones estradiol and progesterone (melatonin increases progesterone and decreases estrogens). Low melatonin caused by pineal calcification has been associated with many different dysfunctions and diseases such as immune dysfunction, neurodegenerative disorders (Alzheimer's disease, senile dementia), pain disorders, cardiovascular disease, cancers of the breast and prostate, and type 2 diabetes (Hardeland R. Aging and Disease 3 (2): 194-225, 2012). Low melatonin is also thought to contribute to obesity in people with insomnia or those who do night shift work.

If melatonin is taken as a supplement (available OTC) to correct low levels or treat a condition, the timing and dosage are important to its effectiveness, especially as a sleep aid. Response to supplemental melatonin can be very individual. For optimal benefit it is best to work with a health care provider familiar with melatonin dosage and timing. Excessive dosing can result in spillover of melatonin into daylight hours, excessive sleepiness during the day, and disruption of the normal melatonin-cortisol circadian rhythms. This will be seen as very high levels of MT6s in the first and second urine voids, and often carry-over into the evening when levels should be low. Consider dosage reduction if MT6s levels are excessive throughout the daylight hours and this is associated with persistent sleepiness during the day. While MT6s is an excellent surrogate marker for melatonin levels in the circulation, oral melatonin supplementation results in much higher MT6s levels in urine that are NOT reflective of active circulating levels of melatonin, since most of the exogenous oral melatonin is rapidly metabolized by the liver and kidney and excreted into urine.

For more general information about melatonin please see: http://www.nlm.nih.gov/medlineplus/druginfo/natural/940.html