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

MICRO SAMPLE ASSAYS

DRIED URINE | Result | Range | Units

Intermediate Hormones, Dried Urine

Your Hormone Testing at a Glance

Urinary Estrogens

Estradiol *H*
Estrone *H*
Estriol *H*
E3/(E1+E2) *L*
2-OH Estrone *H*
4-OH Estradiol *H*
4-OH Estrone *H*
16α-OH Estrone *H*
2-MeO Estrone *H*
2-MeO E1/2-OH E1 *H*
Bisphenol A *H*

Urinary Progestogens

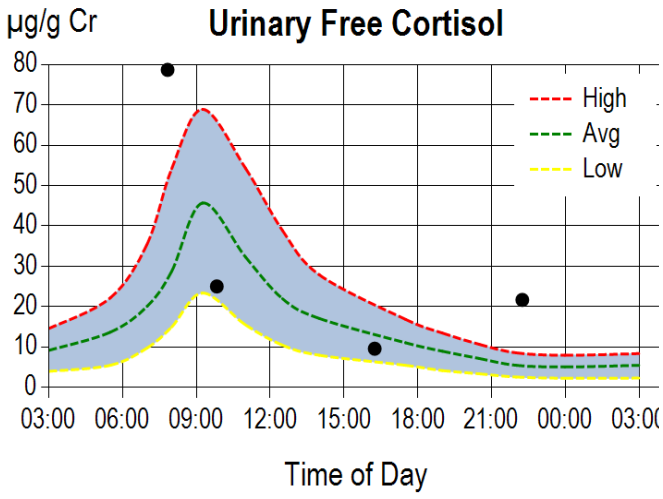
Pregnanediol *L*
Pgdiol/E2 *L*

Urinary Androgens

Testosterone *H*
Epi-Testosterone *H*
5α-DHT *H*

L Items listed in **RED** are reflective of a Low Results *H* Items Listed in **BLUE** are Reflective of a High Result

Your Reported Urinary Free Cortisol Pattern



Tests ordered: 1502

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DRIED URINE TESTING-INTEGRATIVE MEDICINE

Samples Collected: Urine: 00/00/0000 07:50 Urine: 00/00/0000 09:50 Urine: 00/00/0000 16:15 Urine: 00/00/0000 22:15

Test Name	Result		Range
Urinary Estrogens (µg/g Cr)			
Estradiol (Urine)	4.39	H	0.78-1.79 Premeno-luteal or ERT
Estrone (Urine)	17.58	H	2.27-5.22 Premeno-luteal or ERT
Estriol (Urine)	2.85	H	0.78-1.98 Premeno-luteal or ERT
E3/(E1+E2) (Urine)	0.13	L	>0.3 (> median value)
2-OH Estrone (Urine)	4.16	H	0.70-2.54 Premeno-luteal or ERT
4-OH Estradiol (Urine)	0.47	H	0.10-0.18 Premeno-luteal or ERT
4-OH Estrone (Urine)	1.08	H	0.17-0.47 Premeno-luteal or ERT
16α-OH Estrone (Urine)	1.66	H	0.35-1.07 Premeno-luteal or ERT
2-MeO Estrone (Urine)	2.08	H	0.26-0.68 Premeno-luteal or ERT
2-MeO E1/2-OH E1 (Urine)	0.5	H	0.21-0.38 Premeno-luteal or ERT
4-MeO Estradiol (Urine)	<dl		< 0.04
4-MeO E2/4-OH E2 (Urine)	N/A		0.10-0.29 Premeno-luteal or ERT
Bisphenol A (Urine)	10.30	H	1.11-3.74 Premeno-luteal
Urinary Progestogens (µg/g Cr)			
Pregnanediol (Urine)	318	L	465-1609 Premeno-luteal or PgRT
Pgdiol/E2 (Urine)	72.44	L	1000-1500 (Optimal Luteal Only)
Allopregnanolone (Urine)	3.50		2.23-14.87 Premeno-luteal or PgRT
Urinary Androgens (µg/g Cr)			
DHEA (Urine)	49.63		15.82-129.17 Premeno-luteal or DHEAT
Androstenedione (Urine)	10.43		3.93-13.53 Premeno-luteal or ART
Testosterone (Urine)	5.98	H	1.22-3.97 Premeno-luteal or ART
Epi-Testosterone (Urine)	5.85	H	2.01-4.66 Premeno-luteal
T/Epi-T (Urine)	1.02		0.5-3.0
5α-DHT (Urine)	2.32	H	0.28-1.52 Premeno-luteal or ART
Urinary Glucocorticoids (µg/g Cr)			
Total Cortisol (Urine)	71.73	H	12.26-33.12 Premeno-luteal
Total Cortisone (Urine)	138.51	H	23.27-50.88 Premeno-luteal
Cortisol/Cortisone (Urine)	0.52		0.5-0.7
Tetrahydrocortisol (Urine)	922	H	214-546 Premeno-luteal
Tetrahydrocortisone (Urine)	3698	H	437-1184 Premeno-luteal

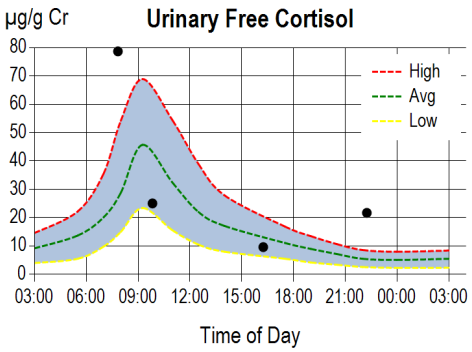
Test Name	Result		Range
Urinary Free Diurnal Cortisol (µg/g Cr)			
Free Cortisol (Urine)	78.66	H	7.8-29.5 (1st Morning)
Free Cortisol (Urine)	25.03		23.4-68.9 (2nd Morning)
Free Cortisol (Urine)	9.61		6.0-19.2 (Evening)
Free Cortisol (Urine)	21.69	H	2.6-8.4 (Night)
Urinary Free Diurnal Cortisone (µg/g Cr)			
Free Cortisone (Urine)	181.28	H	31.6-91.6 (1st Morning)
Free Cortisone (Urine)	265.40	H	63.3-175.8 (2nd Morning)
Free Cortisone (Urine)	86.36		30.6-88.5 (Evening)
Free Cortisone (Urine)	84.70	H	15.5-44.7 (Night)
Urinary Diurnal Melatonin MT6s (µg/g Cr)			
Melatonin (Urine)	16.81	L	18.0 - 40.9 (1st Morning)
Urinary Creatinine (mg/mL)			
Creatinine (pooled) (Urine)	0.73		0.3-2.0
Creatinine (Urine)	1.97		0.3-2.0 (1st morning)
Creatinine (Urine)	0.47		0.3-2.0 (2nd morning)
Creatinine (Urine)	0.63		0.3-2.0 (Evening)
Creatinine (Urine)	1.24		0.3-2.0 (Night)

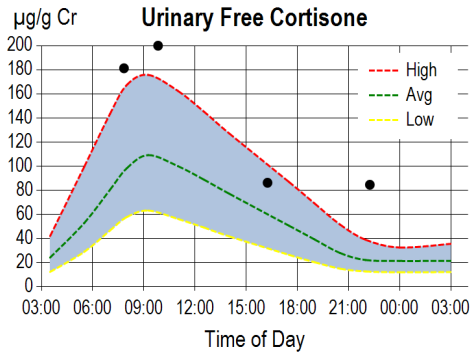
<dL = Less than the detectable limit of the lab.
N/A = Not applicable; 1 or more values used in this calculation is less than the detectable limit.

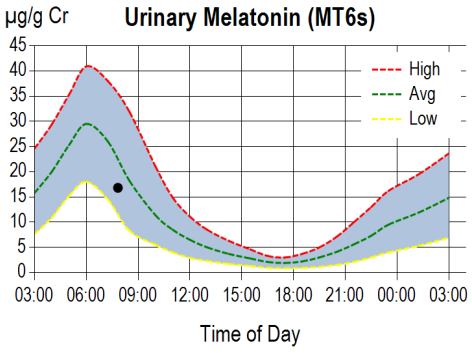
Therapies

oral Vitamin D (unknown type) (OTC) (1 Days Last used)

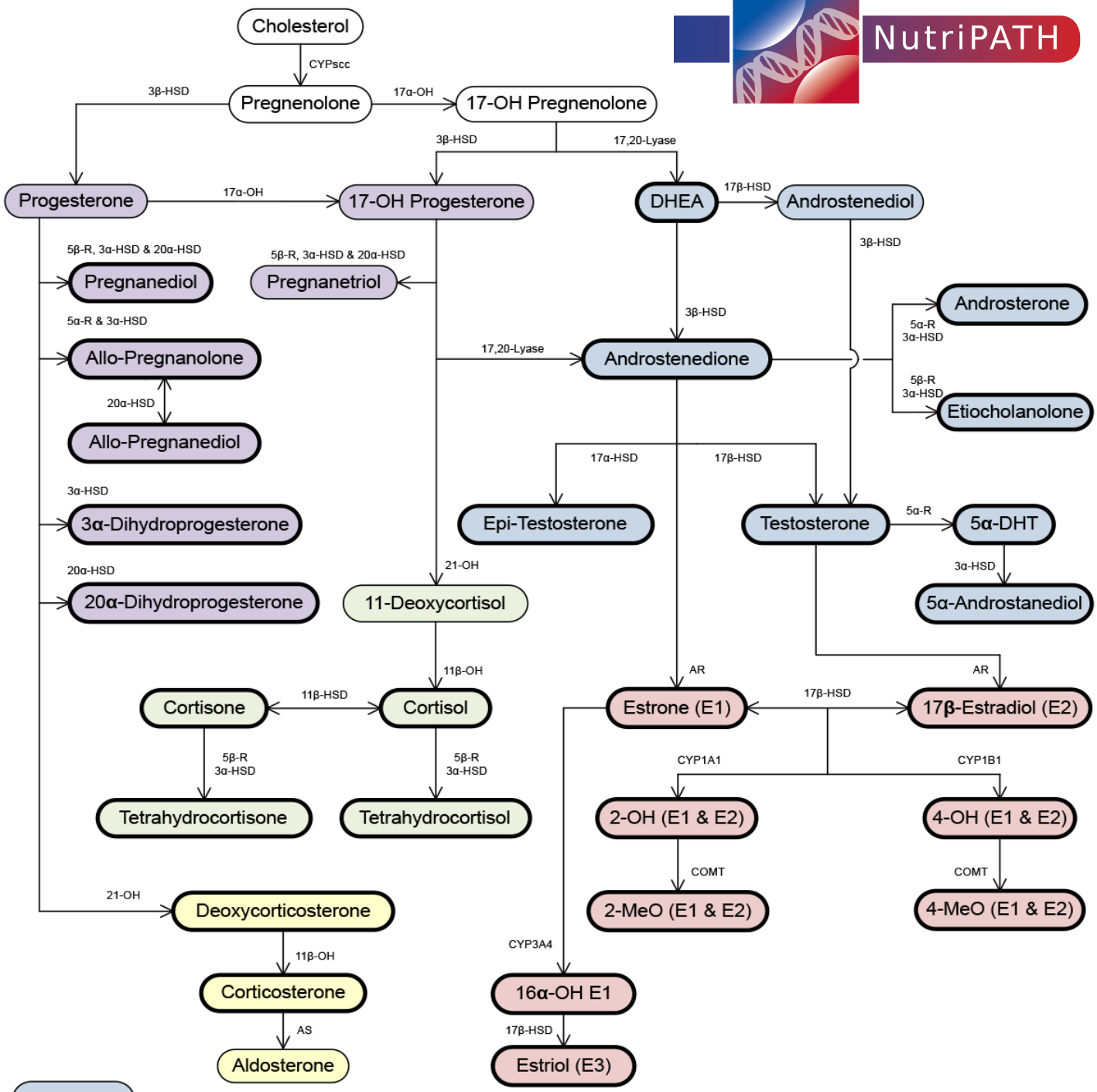
Disclaimer: Graphs below represent hormone levels in testers not using hormone supplementation and are provided for informational purposes only. Please see comments for additional information if results are higher or lower than expected.







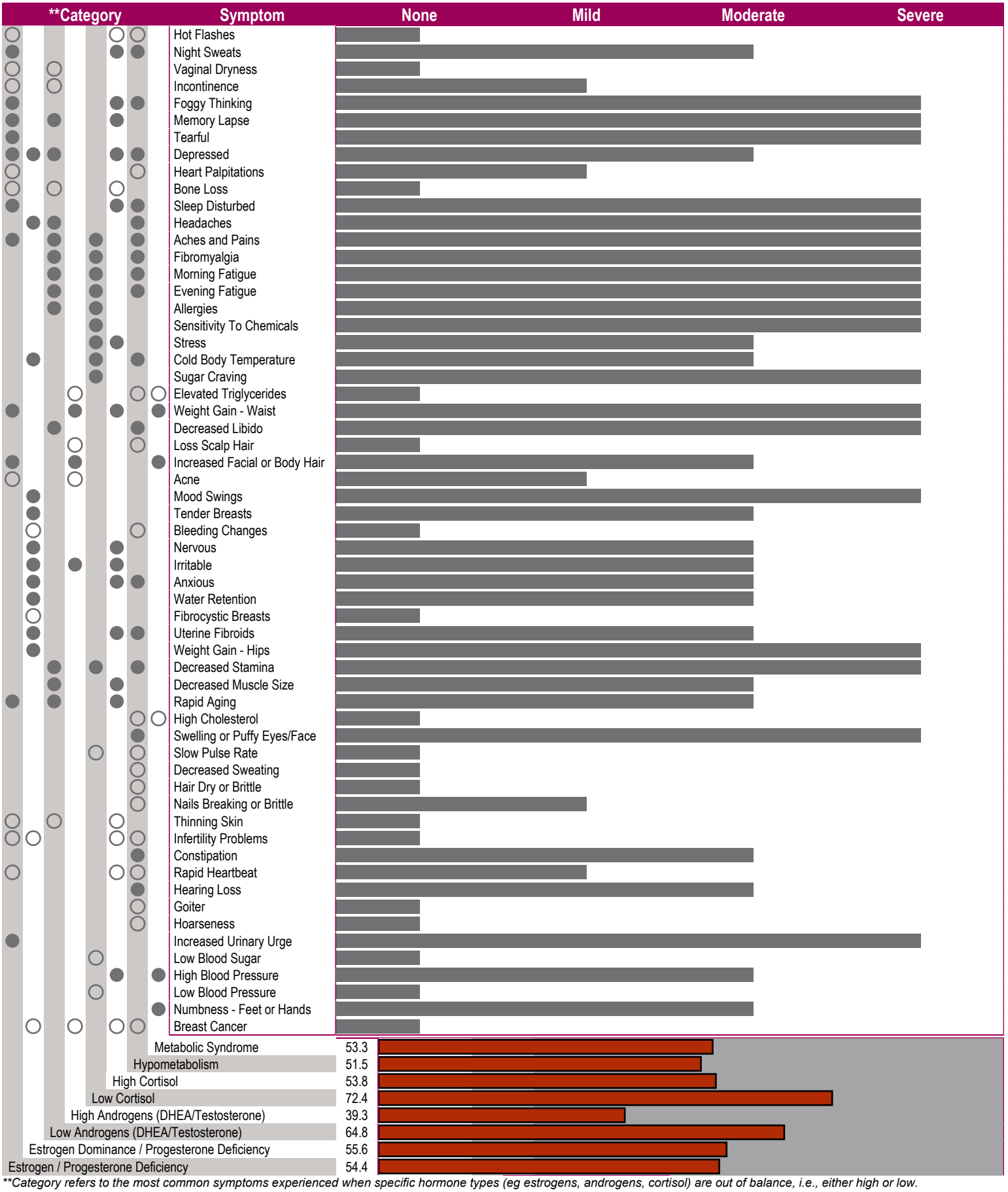
The Steroid Hormone Cascade



Enzyme Abbreviations

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

LAB ID: 0000000 **PATIENT NAME**



***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.*

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Lab Comments

PARENT ESTROGENS (ESTRADIOL-E2, ESTRONE-E1, ESTRIOL-E3)

The parent estrogens are higher than the reference range seen in premenopausal women. Symptoms of estrogen imbalance (dominance) are self-reported as problematic. This occurs most commonly in the teens and then again during the 10 or so years before menopause (perimenopause), when estrogens are produced at higher levels relative to progesterone (low Pgdiol/E2 ratio). Consider means to lower the estrogen burden (diet consisting of more fiber and cruciferous vegetables, less red meat, weight reduction if problematic) and progesterone restoration therapy as this often helps balance symptoms of both estrogen deficiency and excess that occur during these periods of transition.

HYDROXYLATED (CATECHOL) ESTROGENS (2-OH E2 & E1, 4-OH E2 & E1, 16-OH E1) and 2-OH/16-OH RATIO

All of the 2- and 4-hydroxylated estrogens are higher than the reference ranges. If these remain elevated over a prolonged period of time (years) this infers a higher lifetime risk for breast cancer if they are not adequately methylated (see Methylated Hydroxyestrogens below).

The hydroxylation of estradiol and estrone represent the first phase of metabolism and elimination of these estrogens via urine. Following hydroxylation at the 2-, 4-, or -16 position, the estrogens undergo further modification (methylation, sulfation, glucuronidation) that increases their solubility and excretion in urine. The sulfate and glucuronide groups are removed by enzyme hydrolysis, which allows for measurement of the different types of hydroxylated estrogens, in addition to methylation of the hydroxyl groups (see below). The 2- and 4-hydroxylated E1 and E2 are referred to as catechol estrogens.

Research and clinical studies show that the 2-hydroxylated estrogens (2-OH E2 and 2-OH E1) are a safer pathway of hydroxylation than the 4-hydroxyestrogens (4-OH E2 and 4-OH E1), which bind to and damage DNA, leading to mutations that are associated with increased breast cancer risk. For reviews see: Cavalieri EL, Rogan EG Future Oncol 6(1): 75-79, 2010; and Lee, JR, Zava DT What Your Doctor May Not Tell You About BREAST CANCER: How Hormone Balance Can Help Save Your Life: Chapter 7.

2-hydroxylated estrogen metabolism is increased with cruciferous vegetables and extracts of them. The most commonly used are indole-3-carbinol (I3C) and its metabolite diindolylmethane (DIM). Iodine also increases the 2-hydroxylation of estrogens, with a slight increase in 4-hydroxylation (Stoddard FR et.al. Int J Med Sci 5: 189-196, 2008). The more dangerous 4-hydroxylated estrogen metabolism is enhanced by exposure to environmental toxins, mostly petrochemical-based products but also heavy metals, that induce 4-hydroxylation pathway enzymes (1B1), and cause formation of Reactive Oxygen Species (ROS) that co-oxidize the catechol estrogens to much more reactive quinone estrogens. The 4-quinone estrogens, if not inactivated by glutathione, can potentially bind to and damage DNA leading to mutations that may cause cancer.

16-hydroxyestrone is another pathway of estrone metabolism and is a precursor to estriol (see Steroid Hormone Cascade). Early clinical research in humans suggested that a high urinary level of 16-hydroxyestrone relative to 2-hydroxylated estrogens (i.e. a low 2-OH E1 + 2-OH E2/16-OH E1 ratio), was associated with an increased risk of breast cancer in premenopausal women, but not in postmenopausal women. This has remained controversial and newer research suggests that while higher levels of 16-hydroxy estrone may indeed be slightly associated with increased breast cancer risk in premenopausal women, higher levels are, paradoxically, associated with a decreased risk in postmenopausal women (Huang J et.al. Analytica Chimica Acta 711: 60-68, 2012). Overall, more recent studies have not shown the 2/16 ratio to be useful for predicting breast cancer risk.

METHYLATION OF HYDROXYESTROGENS

The methylated forms of the 2-hydroxyestrogens are within normal reference ranges or high (beneficial). In contrast, methylation of the more toxic 4-hydroxyestrogens is low or within the lower quadrant of the reference range (considered higher risk). Adequate methylation of the hydroxyestrogens, and an associated high ratio of 4-hydroxylated estrogens to 4-methoxyestrogens (i.e. 4 MeO-E2/4-OH-E2 and 4-MeO-E1/4-OH-E1) is considered beneficial as this indicates the 4-hydroxyestrogens are rendered inert via methylation, preventing them from oxidizing further to more dangerous 4-estrogen quinones that can form adducts with DNA, causing mutations that can lead to increased cancer risk. The ratios of 4-MeO-E1/4-OH-E1 and 4-MeO-E2/4-OH-E2 are within range, but within the lower quadrant of the reference ranges, indicating that these 4-OH-estrogens are not adequately methylated.

The 2- and 4- hydroxyl estrogens are methylated by the enzyme Catechol-o-Methyl Transferase (COMT), which renders these catechol estrogens inert and harmless (Cavalieri EL, Rogan EG Future Oncol 6(1): 75-79, 2010). In this form the methylated catechol estrogens are rapidly excreted in urine. However, if methylation pathways are inadequate due to low levels of COMT, or lack of precursors of methylation (i.e. vitamins B6, B12, folate, betaine), the 2- and 4-hydroxyl estrogens can oxidize to 4-estrogen quinones that bind to DNA, forming adducts that can lead to permanent mutations, and eventually to cancer.

Many studies have shown that high urinary levels of these 4-hydroxyestrogens (4-OH-E2 and 4-OH-E1) are associated with increased breast cancer risk if they are not inactivated by methylation, or the more toxic down-stream oxidized 4-quinone estrogens are not inactivated by glutathione sulfation. If glutathione is low the 4-quinone estrogens are less likely to be detoxified (inactivated) and have potential to damage cells/DNA in close proximity to their formation (i.e. the breast cell/DNA). Maintaining adequate glutathione is key to preventing buildup of toxic/mutagenic 4-quinone estrogens, should they form due to poor methylation pathways. If 4-OH-estrogens are high and not well methylated consider avoiding trans-hydrogenated fats and eliminate heavy metals that cause the formation of Reactive Oxygen Species (ROS) that oxidize lipids. Supplementation with essential elements such as selenium and iodine will also help reduce formation of oxidized lipids, which co-oxidize 4-OH-estrogens to 4-quinone estrogens.

BISPHENOL A (BPA)

Bisphenol A (BPA) is very elevated. BPA is an endocrine disrupting chemical (EDC) derived from plastics used for making bottles, wraps for foods, and linings for food cans. BPA is not retained in the body for a prolonged period of time and is rapidly excreted into urine. High urinary levels of BPA indicate recent exposure to plastics that released excessive amounts of BPA into food or beverages consumed in the past 24-48 hr.

BPA acts as an EDC by binding to a activating both membrane and nuclear estrogen receptors in a manner similar to estradiol. Thus by mimicking the actions of endogenous estrogens, high levels of BPA can contribute to symptoms of estrogen dominance. High BPA levels have been associated with increased risks for many different health issues, including diabetes, breast cancer, and prostate cancer. When BPA levels are elevated, identification of its source and reducing exposure is worth considering.

PROGESTERONE SURROGATE METABOLITE (PREGNANEDIOL)

Pregnanediol is lower than the expected reference range for a premenopausal woman during the luteal phase of the menstrual cycle. Pregnanediol is a metabolite of progesterone that is excreted into urine and used as a surrogate marker for progesterone production by the ovaries. Levels of pregnanediol closely parallel those of progesterone in serum.

Low pregnanediol 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) and is associated with normal levels of estrogens, but is not followed by sufficient ovarian progesterone synthesis to maintain a pregnancy, should it occur. Luteal insufficiency can occur throughout the years of menstruation, but is more common in the latter years of premenopause (age 45-55), often referred to as perimenopause, before the transition to menopause.

Low pregnanediol (i.e. progesterone) 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. The normal to high estrogens, very low progesterone, and high testosterone seen in these test results points to PCOS as a possible cause of this abnormal hormone pattern.

Progesterone therapy, in concert with reduction in simple carbohydrates, stress reduction (lowers cortisol which at high levels can disrupt normal synthesis of sex-steroids) and exercise often helps correct this condition. Synthetic progestins, found in oral contraceptives and some forms of Hormone Replacement Therapy (HRT) can often help correct symptoms/conditions associated with PCOS by lowering androgens (testosterone); however, this can exacerbate insulin resistance and lead to weight gain, particularly around the waist.

ANDROGEN PRECURSORS (ANDROSTENEDIOL, DHEA)

Androstenedione and DHEA(S) are within expected reference ranges seen in premenopausal women.

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. Androstenedione is converted into the androgens, testosterone and Epi-testosterone in near equal amounts in most individuals, or into estrone. More conversion to estrone occurs in individuals with higher amounts of adipose (fat) tissue, which contains high levels of aromatase, an enzyme that converts androgens to estrogens.

ANDROGENS (TESTOSTERONE-T, DIHYDROTESTOSTERONE-DHT, EPI-TESTOSTERONE-EPI-T)

Testosterone (T) and its downstream metabolite, 5-alpha DHT, are higher than the reference ranges for a premenopausal woman. DHT is the most potent of the androgens and is formed from testosterone within target cells via the enzyme 5 alpha reductase. There it binds to androgen receptors to activate androgen-specific gene sites. High levels of these androgens are often associated with symptoms of androgen excess (e.g. loss of scalp hair, increased facial/body hair, and/or acne), especially when estrogens and progesterone (pregnanediol) are low. Both estrogens and progesterone are androgen antagonists. Epi-testosterone (Epi-T) is also elevated, which indicates that the high T is coming from an endogenous precursor (e.g. androstenedione or DHEA). T/Epi-T ratio < 3 usually indicates endogenous testosterone production whereas a ratio > 3 usually indicates testosterone therapy/exposure. Epi-testosterone (Epi-T) and testosterone (T) are created in about equal amounts from androstenedione and DHEA. The ratio of T/Epi-T should be about 1 under normal circumstances, but normally ranges from about 0.5-2. The T/Epi-T ratio in this individual is < 3 supporting the concept that T is derived from endogenous sources (ovaries or adrenal glands). An elevated androstenedione with a low or normal DHEA would indicate the T source is ovarian, whereas a low or normal androstenedione and an elevated DHEA would indicate the source is likely adrenal, or DHEA supplementation.

Androgens 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. Androgens are also precursors to the estrogens, estradiol and estrone. The most potent of the androgens is dihydrotestosterone (DHT), which is created from testosterone via 5a reductase. Testosterone itself is derived mostly from androstenedione and DHEA. In premenopausal women about half of the testosterone is derived from androstenedione produced by the ovaries, and the other half from peripheral conversion of DHEA manufactured in the adrenals.

In premenopausal women high androgens, as seen in this individual, is usually associated with Polycystic Ovarian Syndrome (PCOS), which is closely associated with insulin resistance and metabolic syndrome. If left untreated this often progresses to diabetes and its adverse health outcomes. This condition is usually associated with one or more of the following: excessive weight, high stress, poor eating habits, sedentary lifestyle, poor sleep, and various hormonal imbalances (high insulin, high estrogens/low progesterone, high androgens, high cortisol, low thyroid). Correcting these hormonal imbalances in combination with improved lifestyle modifications usually helps reverse insulin resistance, metabolic syndrome, and some of the associated hormonal imbalances (e.g. high androgens and high androgen symptoms).

TOTAL GLUCOCORTICOIDS

Total cortisol (F) and cortisone (E), and their down-stream metabolites, tetrahydrocortisol (THF) and tetrahydrocortisone (THE), are higher than the expected reference ranges. The total levels of these glucocorticoids are determined from the average of four urine collections throughout the day and are very similar to 24 hour urine values.

A high cortisol is a normal and healthy response to an acute stressor; however a 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. 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. Therefore, means to lower stress(ors) and cortisol are worth considering.

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 (F) AND URINARY FREE CORTISONE (E)

Urinary free cortisol (F) and cortisone (E) are very elevated in the first morning urine void and also elevated before bed at night. High levels of F and E at these time points indicate that cortisol is highest during sleeping hours, when it should be at the lowest level. F and E levels are also elevated throughout most of the day. High F and E throughout most of the day are consistent with this individual's self-reporting of excessive stress.

In a healthy individual without significant stressors, cortisol begins to rise in the morning shortly after awakening and steadily

drops throughout the day, reaching the lowest level during sleep in the very early morning about 2 am. The first urine void is representative of the overnight production of cortisol during the sleeping hours. The second void, which optimally is collected about 2 hours after waking, is representative of the awakening response and should be the highest level of the four collections. It is equivalent to a first morning saliva or blood cortisol measurement about 30 minutes after awakening. The rise in F and E seen from the first to the second morning urine voids are equivalent to a salivary Cortisol Awakening Response (CAR). If the adrenal glands are functioning normally, and stressors are minimal the second void should be significantly higher than the first void, but remain within the reference range (note that F and E are both higher in the first morning void than the second void).

Higher first morning F and E are usually the result of stressors that occur during the night. The most common stressors that can raise cortisol levels include psychological stressors (emotional), physical insults (surgery, injury, diseases), chemical exposure (environmental pollutants, excessive medications), hypoglycemia (low blood sugar), and pathogenic infections (bacterial, viral, fungal). Chronic and persistent stressors and chronic high cortisol production by the adrenal glands over a prolonged period of time (months/years) can lead to excessive breakdown of normal tissues (muscle wasting, thinning of skin, bone loss) and immune suppression. Chronic high cortisol, particularly if it is elevated throughout the day or high at night, is associated most commonly with symptoms and conditions such as sleep disturbances, vasomotor symptoms (hot flashes and night sweats despite normal or high estrogen levels), fatigue and depression, weight gain in the waist, and bone and muscle loss. Many of these symptoms associated with high cortisol are self-reported.

For additional information about strategies for supporting adrenal health and reducing stressors, 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; "Thyroid Power", by Richard Shames, MD. “The Role of Stress and the HPA Axis in Chronic Disease Management” by Thomas Guilliams, PhD.

MELATONIN METABOLITE 6-SULFATOXYMELATONIN (MT6s)

The urine melatonin metabolite MT6s is low in the first morning void. MT6s in the first morning void is representative of the average melatonin produced throughout the night, which is usually a 6-8 hr interval without light. The first void should have the highest level of melatonin since it usually represents the longest period of darkness, which is necessary for melatonin synthesis. Melatonin is produced by the pineal gland in the brain where it is released into the circulation and rapidly enters tissues throughout the body to carry out its restorative properties. Melatonin synthesis decreases with aging; calcification of the pineal gland, which has been associated with cancers such as breast cancer, can result in very low production of melatonin.

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 a susceptibility to obesity in people with insomnia or those who do night shift work. The WHO’s International Agency for Research on Cancer has concluded that “shift work that involves circadian disruption is probably carcinogenic to humans”, because of the suppression of melatonin production by exposure to light during the night. Melatonin levels tend to be low and have flat circadian rhythms in individuals with cancers of the breasts and prostate.

Because melatonin in this individual’s first morning void is low consider melatonin supplementation (see: http://www.nlm.nih.gov/medlineplus/druginfo/natural/940.html). Treatment with exogenous melatonin has been found useful in people with circadian rhythm sleep disorders, such as delayed sleep phase disorder, jet lag, shift worker disorder, and the non-24-hour sleep-wake disorder most commonly found in totally blind individuals; however, its utility for the treatment of insomnia is not established and remains controversial. 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, causing 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 urine voids. If melatonin is not appropriately metabolized and cleared, higher levels of MT6s will also be seen throughout the day when measuring the four time point circadian pattern of melatonin.