NutriPATH
Integrative Pathology Services
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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
Androgen Elite, Dried Urine			
Dried Urine Hormone Comments	Please refer to PDF attached.		

Patient Name: TEST TEST **Samples Collected** Urine - 00:00 Urine - 00:00 Urine - 00:00 Urine - 00:00

TEST NAME	RESULTS | 10/30/18	RANGE
Urinary Estrogens		
Estradiol	0.35	0.18-0.49 µg/g Cr
Estrone	0.88	0.57-1.67 µg/g Cr
Estriol	0.30	0.18-0.64 µg/g Cr
2-OH Estradiol	0.05	0.04-0.14 µg/g Cr
2-OH Estrone	0.31	0.16-0.48 µg/g Cr
4-OH Estradiol	0.04	0.03-0.08 µg/g Cr
4-OH Estrone	0.07	0.04-0.10 µg/g Cr
16α-OH Estrone	0.11	0.06-0.21 µg/g Cr
2-MeO Estradiol	0.02	0.01-0.03 µg/g Cr
2-MeO Estrone	0.09	0.05-0.15 µg/g Cr
2-MeO E1/2-OH E1	0.29	0.20-0.38
4-MeO Estradiol	0.01	<0.04 µg/g Cr
4-MeO Estrone	<0.01	<0.04 µg/g Cr
4-MeO E1/4-OH E1	N/A	0.05-0.17
4-MeO E2/4-OH E2	0.25	0.06-0.47
Bisphenol A	1.57	0.97-2.31 µg/g Cr
Urinary Progestogens		
Pregnanediol	49	47-140 µg/g Cr

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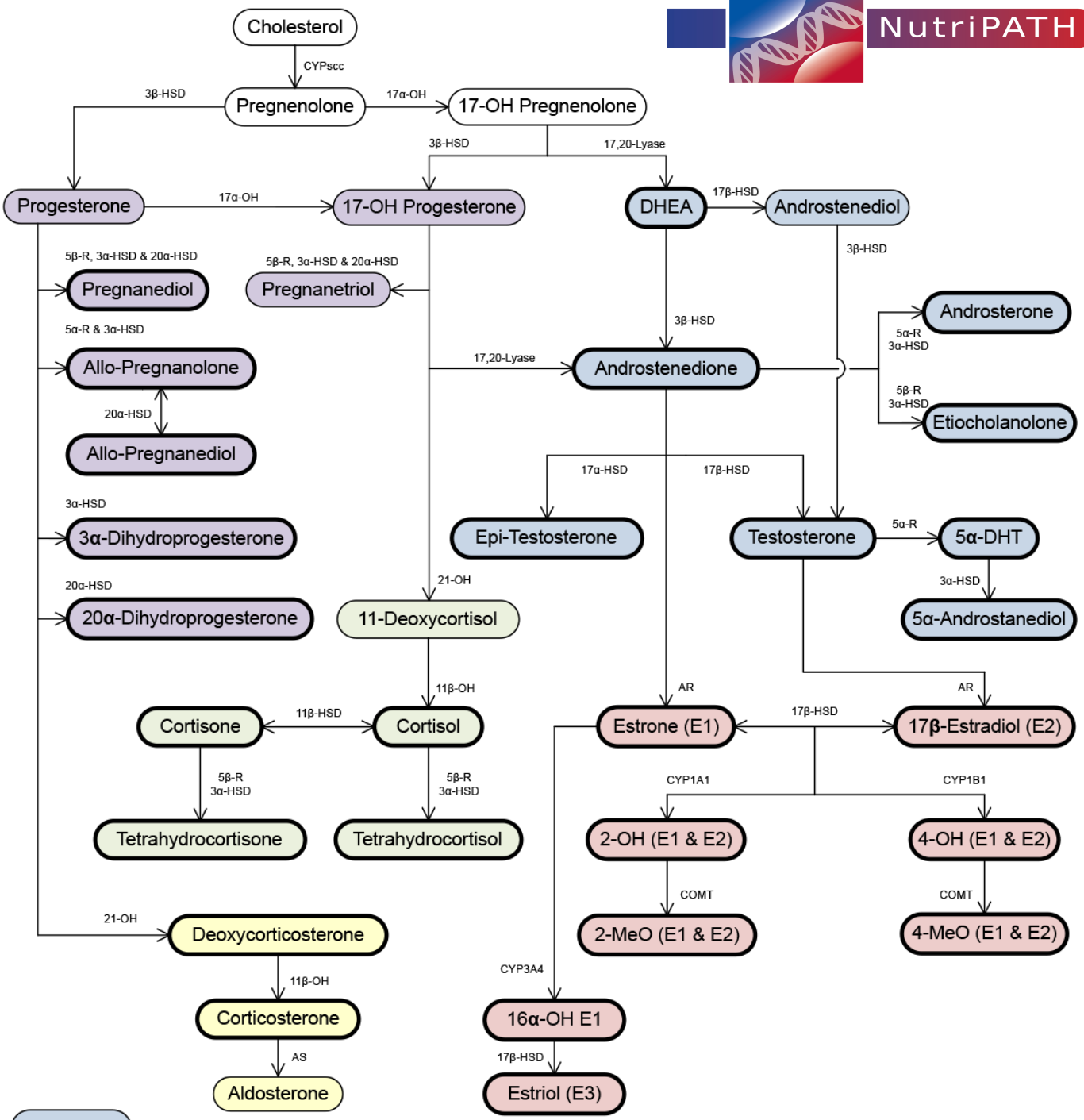
TEST NAME	RESULTS | 10/30/18	RANGE
Urinary Progestogens		
Allopregnanolone	0.13 L	0.32-1.20 µg/g Cr
Allopregnanediol	2.45	1.57-6.82 µg/g Cr
3α-Dihydroprogesterone	0.22	0.19-0.73 µg/g Cr
20α-Dihydroprogesterone	0.44 L	0.51-2.97 µg/g Cr
Deoxycorticosterone	0.82	0.28-1.25 µg/g Cr
Corticosterone	2.39	1.95-8.22 µg/g Cr
Urinary Androgens		
DHEA	11.96	9.01-93.80 µg/g Cr
Androstenedione	4.80	2.12-9.51 µg/g Cr
Androsterone	950 H	302-724 µg/g Cr
Etiocholanolone	430	279-775 µg/g Cr
Testosterone	18.94 H	3.81-14.21 µg/g Cr
Epi-Testosterone	7.15	3.15-8.85 µg/g Cr
T/Epi-T	2.65	0.5-3.0
5α-DHT	3.80 H	0.71-2.46 µg/g Cr
5α,3α-Androstanediol	25.18 H	9.48-24.96 µg/g Cr
Urinary Glucocorticoids		
Total Cortisol	42.87 H	8.73-28.52 µg/g Cr
Total Cortisone	56.13 H	14.12-42.84 µg/g Cr
Cortisol/Cortisone	0.76 H	0.5-0.7
Tetrahydrocortisol	989 H	201-597 µg/g Cr
Tetrahydrocortisone	1714 H	330-1126 µg/g Cr
Urinary Creatinine		
Creatinine (pooled)	2.58 H	0.3-2.0 mg/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

None Indicated

The Steroid Hormone Cascade

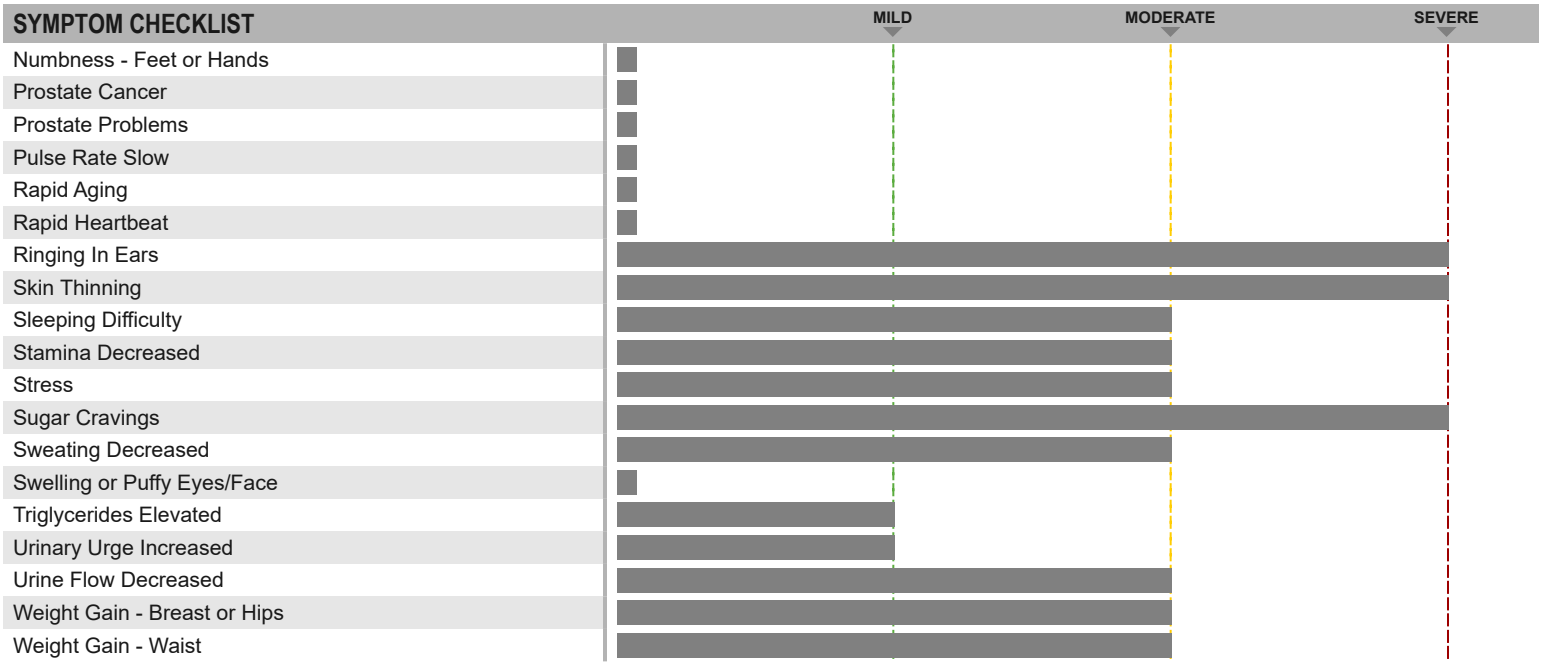


Enzyme Abbreviations

(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

SYMPTOM CATEGORIES	RESULTS | 10/30/18
Estrogen / Progesterone Deficiency	12%
Estrogen Dominance / Progesterone Deficiency	47%
Low Androgens (DHEA/Testosterone)	55%
High Androgens (DHEA/Testosterone)	21%
Low Cortisol	41%
High Cortisol	41%
Hypometabolism	36%
Metabolic Syndrome	39%

SYMPTOM CHECKLIST	MILD	MODERATE	SEVERE
Acne			
Aggressive Behavior			
Allergies			
Anxious			
Apathy			
Blood Pressure High			
Blood Pressure Low			
Blood Sugar Low			
Body Temperature Cold			
Bone Loss			
Burned Out Feeling			
Chemical Sensitivity			
Cholesterol High			
Constipation			
Depressed			
Dizzy Spells			
Erections Decreased			
Fatigue - Evening			
Fatigue - Mental			
Fatigue - Morning			
Flexibility Decreased			
Forgetfulness			
Goiter			
Hair - Dry or Brittle			
Hair or Skin Oily			
Headaches			
Hearing Loss			
Heart Palpitations			
Hoarseness			
Hot Flashes			
Infertility			
Irritable			
Joint Pain			
Libido Decreased			
Mental Sharpness Decreased			
Muscle Size Decreased			
Muscle Soreness			
Nails Breaking or Brittle			
Neck or Back Pain			
Nervous			
Night Sweats			



Lab Comments

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

The parent estrogens (E2, E1, and E3) are within or near the limits of the reference ranges seen in healthy men. While estrogen levels in men are naturally lower than in women, adequate levels of estrogens, particularly the most potent, E2, are important for men's health; they help maintain a healthy skeletal system, brain, and cardiovascular system. Estrogen levels below or above the physiological range can result in adverse health effects. Low estrogens are associated with more accelerated bone loss and risk of fracture, and advanced aging of the brain (Alzheimer's disease and senile dementia) and cardiovascular system. High estrogens are equally deleterious in men and are associated with excessive weight gain, gynecomastia, and overgrowth of the prostate gland (benign prostatic hypertrophy-BPH). Maintaining estrogens within a healthy physiological range is important to optimal health.

Estrogens are down-stream metabolites of androgens (DHEA, androstenedione, and testosterone) and low levels of estrogens, especially in older men, are usually a result of low levels of androgens. Androgen replacement therapy can be problematic when too much of the androgen converts to estrogens instead of DHT. Androgen to estrogen conversion is more likely to occur in men who are overweight with excessive mid-body (belly) fat, which contains high levels of the enzyme aromatase that converts androgens to estrogens (e.g. testosterone to estradiol).

HYDROXYLATED (CATECHOL) ESTROGENS (2-OH E2 & E1, 4-OH E2 & E1)

The hydroxylated estrogens are all within or very near the expected reference ranges for a male.

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.

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 if not inactivated by methylation can be further oxidized to estrogen quinones that bind to and damage DNA, leading to mutations that are associated with increased risk of estrogen-sensitive tissues (e.g. prostate, breasts). For this reason it is important to keep the levels of the parent estrogens (estradiol and estrone) as well as their down-stream hydroxylated forms within physiological levels to avoid toxic effects from them. For reviews see: Cavalieri EL, Rogan EG Future Oncol 6(1): 75-79, 2010.

The safer 2-hydroxylation of estradiol and estrone 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). While higher levels

of 16-hydroxy estrone may be slightly associated with increased breast cancer risk in premenopausal women, but paradoxically lower risk in postmenopausal women (Huang J et.al. Analytica Chimica Acta 711: 60-68, 2012), very little is known about the role of this estrogen, or its down-stream metabolite, estriol, in risk for prostate cancer.

METHYLATION OF HYDROXYESTROGENS

The methylated forms of the 2- and 4-hydroxyestrogens (2MeO-E2, 2MeO-E1, 4MeO-E2, 4MeO-E1) are within or near the expected reference ranges for a male. Methylated estrogens within the higher range are considered beneficial, especially for the more geno-toxic 4-OH-estrogens (4-OH-E2, 4-OH-E1). High levels of the 4-OH-estrogens and poor methylation of them (i.e. low ratios of 4-MeO-E2/4-OH-E2 and 4-MeO-E1/4-OH-E1) is associated with higher risk for cancers of the breasts and prostate. A higher ratio is considered beneficial as this indicates the 4-OH-estrogens are neutralized by methylation.

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 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 take a more insidious and dangerous pathway of metabolism, which is oxidation of the 4-hydroxylated estrogens (4-OH-E1 and 4-OH-E2) to their respective quinones.

Estrogen quinones, especially the 4-quinone of estradiol and estrone, are highly electrophilic and bind to DNA, forming adducts that lead to permanent mutations in the DNA. Many studies have shown that high urinary levels of these 4-quinones of estradiol and/or estrone are associated with increased breast cancer risk, and research also suggests this same mechanism is responsible for increased risk for prostate cancer. The 2- and 4-hydroxy estrogens are converted to their more dangerous oxidized quinone forms under oxidizing conditions in the cell, and this occurs rapidly in the presence of oxidized lipids, especially those from trans-hydrogenated fats.

These estrogen quinones, like all oxidized and electron-hungry molecules in the body are inactivated when bound to glutathione, the most ubiquitous antioxidant in the body. However, if glutathione is low, due to insufficient levels of minerals (selenium, iodine) and vitamins (C and E), the 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 or prostate cell/DNA).

BISPHENOL A (BPA)

Bisphenol A (BPA) is within reference range. 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 (PREGNANE AND PREGNENE) METABOLITES

Pregnanediol (surrogate for progesterone) and the pregnane and pregnene category of progesterone metabolites are low or within the lower end of the expected references ranges for a male.

In males, progesterone and its down-stream metabolites are much lower than levels found in premenopausal women during the luteal phase of the menstrual cycle, when the ovaries produce large amount of progesterone. Levels of these progesterone metabolites seen in males are similar to, or slightly higher than, levels as seen in postmenopausal women and women during the follicular phase of the menstrual cycle.

Progesterone itself is not found in urine, which is likely related to its very nonpolar nature and preference for excretion in bile/feces. Pregnanediol (PgDiol) is the main metabolite of progesterone that is mostly glucuronidated and then excreted in urine. PgDiol excreted into urine is used as a surrogate marker of progesterone production by the adrenal glands in males and females. Thus, adequate levels of PgDiol and its down-stream metabolites (see Steroid Hormone Cascade), indicate adequate adrenal production of progesterone in males. When PgDiol is low this may indicate that precursors such as pregnenolone are also low.

In addition to Pgdiol, four other progesterone metabolites are tested in the urine metabolite profile. These include allopregnanolone, allopregnanediol, 20-alpha-dihydroprogesterone, and 3-alpha-dihydroprogesterone. The only one of these that likely is relevant to males is allopregnanolone, which is an anxiolytic neurosteroid that binds to brain GABA receptors, resulting in a calming (sleep inducing) effect. Low levels of this progesterone metabolite may result in more sleep problems. Progesterone is also a precursor to cortisol and low levels of progesterone are associated with low levels of cortisol. If cortisol is low consider pregnenolone or progesterone supplementation in addition to other adrenal support.

PROGESTERONE METABOLITES: MINERALCORTICOID PRECURSORS

Deoxycorticosterone (DOC) and corticosterone (CC) are within expected reference ranges for a male. Both DOC and CC are down-stream metabolites of progesterone, which is produced predominately in the adrenal glands in males.

DOC is a weak mineralcorticoid and DOC and CC are precursors to the more potent mineralcorticoid aldosterone (see Steroid Hormone Cascade), which regulates blood pressure via sodium and potassium retention.

ANDROGEN PRECURSORS (ANDROSTENEDIOL, DHEA)

The androgen precursors, androstenedione and DHEA, are within normal reference ranges for a male. Androstenedione is produced in the adrenal glands and testes. 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 the estrogen, estrone, occurs in individuals with higher amounts of adipose (fat) tissue. DHEA is an androstenedione precursor and is commonly used as a supplement to raise testosterone levels in women; however, this does not raise testosterone levels in men.

DHEA/ANDROSTENEDIONE METABOLITES: (ANDROSTERONE, ETIOCHOLANOLONE)

Etiocholanolone is within normal reference range, whereas, androsterone is elevated. Both are downstream metabolites of DHEA and androstenedione (see Steroid Hormone Cascade). The levels of androsterone and etiocholanolone help determine relative 5 alpha and 5 beta reductase activities. 5-alpha and 5-beta reductases are responsible for formation of androsterone and etiocholanolone, respectively.

Higher androsterone seen in these test results is reflective of higher 5 alpha reductase activity. Higher levels of other downstream metabolites of 5 alpha reductase (e.g. dihydrotestosterone-DHT and 5a3a-androstanediol-Adiol), are often seen in concert with high androsterone. If levels of androsterone, DHT, and Adiol are high, this indicates overall high 5 alpha reductase activity. This is often associated with symptoms of androgen excess when estrogens remain low.

Higher androsterone indicates that the 5 alpha reductase, which is the same enzyme that converts T to DHT, dominates. Excessive DHT, in combination with high estrogens, is associated with hyperproliferation of the prostate gland, and increased lifetime risk for prostate cancer. In contrast to high androsterone, high etiocholanolone, relative to androsterone is reported to prevent cancer proliferation by inhibiting glucose utilization, essential for tumor growth. Therefore, higher levels of etiocholanolone, as a result of higher DHEA/androstenedione and 5 beta reductase, are associated with a lower cancer risk.

ANDROGENS (TESTOSTERONE: T; EPI-TESTOSTERONE: EPI-T; DIHYDROTESTOSTERONE: DHT

Testosterone (T) is higher than the reference range and its inert epimer, epi-testosterone (Epi-T), is within normal to high-normal range. The T/EpiT ratio is within expected range. When the T/Epi-T ratio is > 3 this often indicates supplementation with exogenous T, or a precursor such as DHEA. DHT, the more potent down-stream metabolite of T is within normal range, indicating lower 5-alpha reductase activity, which is the intracellular enzyme that converts T to DHT.

T, Epi-T, and DHT are normally within the higher normal reference ranges in healthy young males following puperty, and levels of these androgens progressively drop with age. While androgens naturally decline with age, they can drop more rapidly when the body is exposed to stressors (psychological, physical, surgical, pathogens), sleep deprivation, excessive estrogens, and some medications (opioids, glucocorticoids).

The most potent of the androgens is dihydrotestosterone (DHT), which is created from testosterone via the enzyme 5a reductase. DHEA or T therapy can sometimes lead to excessive levels of either DHT or estradiol, both down-stream metabolites of T via the enzymes 5-alpha reductase and aromatase, respectively. These enzymes are higher in tissues and organs such as the skin, seminal vessicles, prostate, and other organs such as the brain. Endogenous testosterone is derived mostly from androstenedione and DHEA. In men, most of the testosterone is produced in the testes and a much smaller portion is derived from androstenedione in the adrenal glands.

Testosterone, and particularly its more potent down-stream metabolite DHT, are important anabolic hormones that help to maintain both physical and mental health. They help prevent fatigue, help to maintain a normal sex drive, increase the strength of all structural tissues (skin, bone, muscles, heart) and prevent depression and mental fatigue. Testosterone deficiency, particularly when coupled with high estrogens, is more commonly associated with symptoms such as decreased sex drive, memory lapses, grumpiness, thinning skin, weight gain in the hips and thighs (mostly from high estrogens) and loss of muscle and bone mass. Estrogens in excess can block the beneficial effects of T and DHT.

5-ALPHA 3-ALPHA ANDROSTANEDIOL (ADIOL)

The downstream metabolite of DHT, 5-alpha 3-alpha androstanediol (Adiol), is within the high-normal to high reference range. Elevated Adiol is usually associated with higher levels of DHT and androsterone, as well as their precursors DHEA, androstenedione, and testosterone. Adiol is considered a neuroactive steroid that passively enters the brain from the bloodstream through the blood brain barrier. Thus, levels in body fluids outside the brain (blood, urine, saliva) are likely reflective somewhat of levels available to the CNS. Some researchers have suggested that high Adiol, resulting from high testosterone therapy, through its activation of the pleasure/reward dopaminergic pathways, is responsible for addictive effects of high dose androgens (Frye CA. Pharmacol Biochem Behav 86: 347-367, 2007).

Adiol binds to GABAa and dopaminergic receptors in the brain. It has a similar anxiolytic (calming) effects, albeit weaker than allopregnanolone, the 5-alpha 3-alpha metabolite of progesterone. Adiol also interacts with the dopaminergic pathways in the brain and is associated with the dopamine pleasure and reward pathway. Thus, high levels of Adiol are more likely to be associated with conditions/symptoms (addiction, pleasure-thrill seeking behaviors) common to high dopamine and over-activation of the dopaminergic neurons.

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, suggesting some type of adrenal stressor. 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. High cortisol is consistent with self-reported symptoms characteristic of this condition.

While a high cortisol is a normal and healthy response to an acute stressor, a persistent stressor and chronic high cortisol 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.

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.