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

DRIED URINE -INTEGRATIVE MEDICINE

Estrogen Elite, Dried Urine

Samples Collected: Urine: 00/00/0000 08:00 Urine: 00/00/0000 10:00 Urine: 00/00/0000 16:45 Urine: 00/00/0000 20:30

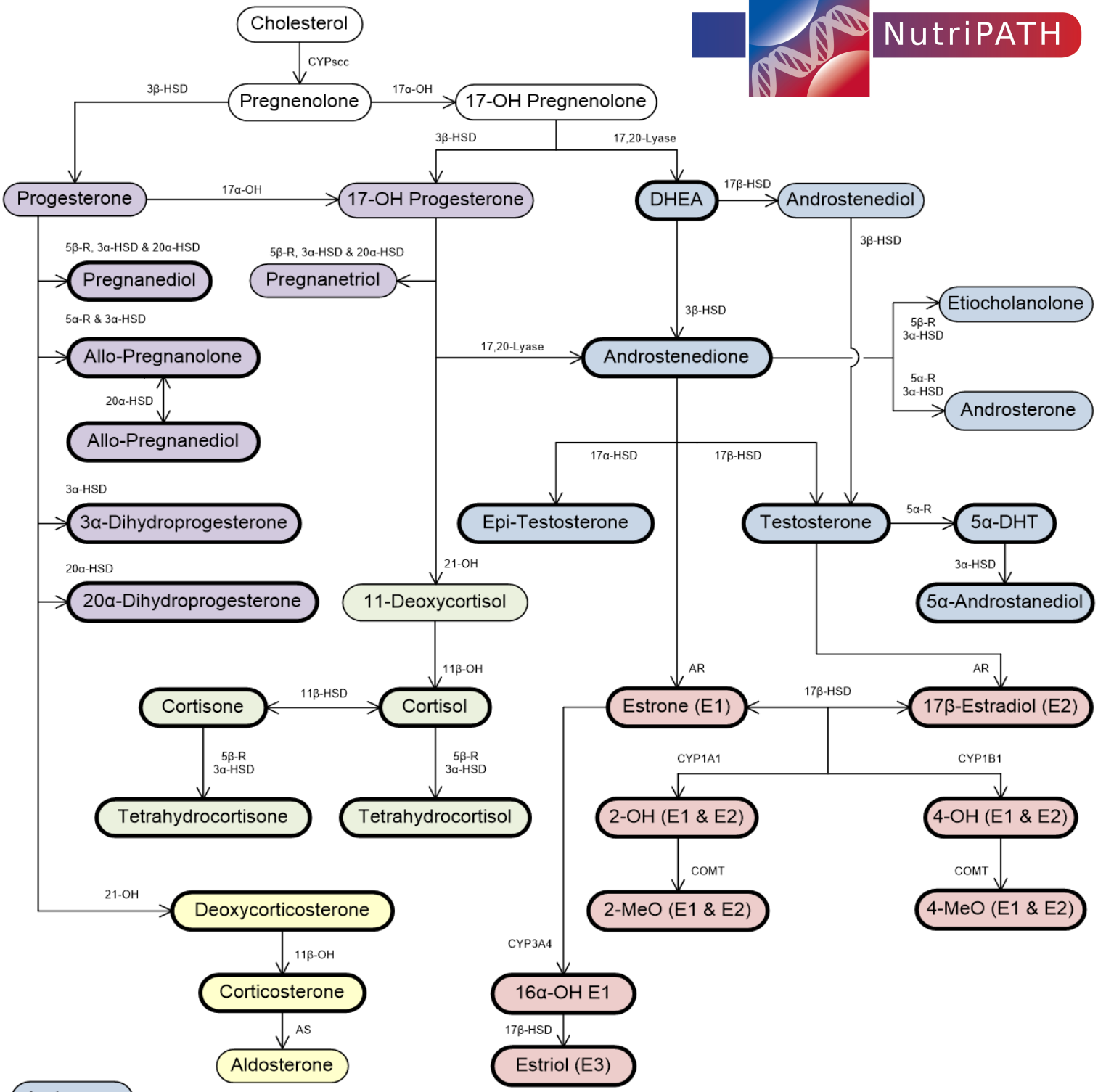
BMI: 00
Height: 0 ft in
Weight: 00 kg

Test Name	Result		Range
Urinary Estrogens (µg/g Cr)			
Estradiol (Urine)	0.29		0.18-0.49
Estrone (Urine)	1.23		0.57-1.67
Estriol (Urine)	1.67	H	0.18-0.64
2-OH Estradiol (Urine)	0.08		0.04-0.14
2-OH Estrone (Urine)	0.37		0.16-0.48
4-OH Estradiol (Urine)	0.03		0.03-0.08
4-OH Estrone (Urine)	0.09		0.04-0.10
16α-OH Estrone (Urine)	0.48	H	0.06-0.21
2-MeO Estradiol (Urine)	0.02		0.01-0.03
2-MeO Estrone (Urine)	0.10		0.05-0.15
2-MeO E1/2-OH E1 (Urine)	0.27		0.20-0.38
4-MeO Estradiol (Urine)	<dl		< 0.04
4-MeO Estrone (Urine)	<dl		< 0.04
4-MeO E1/4-OH E1 (Urine)	N/A		0.05-0.17
4-MeO E2/4-OH E2 (Urine)	N/A		0.06-0.47
Bisphenol A (Urine)	2.81	H	0.97-2.31
Urinary Progestogens (µg/g Cr)			
Pregnanediol (Urine)	78		47-140
Allopregnanolone (Urine)	0.48		0.32-1.20
Urinary Androgens (µg/g Cr)			
DHEA (Urine)	10.39		9.01-93.80
Androstenedione (Urine)	5.08		2.12-9.51
Testosterone (Urine)	9.91		3.81-14.21
Epi-Testosterone (Urine)	6.10		3.15-8.85
T/Epi-T (Urine)	1.62		0.5-3.0
5α-DHT (Urine)	0.98		0.71-2.46
Urinary Creatinine (mg/mL)			
Creatinine (pooled) (Urine)	1.08		0.3-2.0

<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.

Tests ordered: 1505

The Steroid Hormone Cascade



Androgens

Estrogens

Glucocorticoids

Mineralocorticoids

Progestogens

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	Symptom	None	Mild	Moderate	Severe
	Burned Out Feeling				
	Apathy				
	Difficulty Sleeping				
	Increased Forgetfulness				
	Decreased Mental Sharpness				
	Depressed				
	Mental Fatigue				
	Irritable				
	Nervous				
	Anxious				
	Morning Fatigue				
	Evening Fatigue				
	Decreased Stamina				
	Decreased Muscle Size				
	Sore Muscles				
	Increased Joint Pain				
	Decreased Flexibility				
	Neck or Back Pain				
	Weight Gain - Breast or Hips				
	Weight Gain - Waist				
	Elevated Triglycerides				
	Sugar Craving				
	Heart Palpitations				
	Dizzy Spells				
	Headaches				
	Ringing In Ears				
	Cold Body Temperature				
	Allergies				
	Sensitivity To Chemicals				
	Decreased Erections				
	Decreased Libido				
	Prostate Problems				
	Decreased Urine Flow				
	Increased Urinary Urge				
	Hot Flashes				
	Night Sweats				
	Bone Loss				
	Stress				
	Rapid Aging				
	High Cholesterol				
	Swelling or Puffy Eyes/Face				
	Slow Pulse Rate				
	Decreased Sweating				
	Hair Dry or Brittle				
	Nails Breaking or Brittle				
	Thinning Skin				
	Infertility Problems				
	Constipation				
	Rapid Heartbeat				
	Hearing Loss				
	Goiter				
	Hoarseness				
	Low Blood Sugar				
	High Blood Pressure				
	Low Blood Pressure				
	Numbness - Feet or Hands				
	Oily Skin or Hair				
	Acne				
	Aggressive Behavior				
	Prostate Cancer				

Metabolic Syndrome	57.6
Hypometabolism	38.1
High Cortisol	59.7
Low Cortisol	39.2
High Androgens (DHEA/Testosterone)	33.3
Low Androgens (DHEA/Testosterone)	59.3
Estrogen Dominance / Progesterone Deficiency	65.0
Estrogen / Progesterone Deficiency	19.0

***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

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

The parent estrogens E2 and E1 are within the llimits of the reference ranges. Estriol, on the other hand, is elevated, as is 16-OH estrone, a precursor to estriol. High 16-OH estrone (upper quadrant of the reference range) has been correlated with increased risk for prostate cancer (Barba M. J Exp Clin Cancer Res 28: 135, 2009), and may have contributed to this individuals diagnosis of prostate cancer. High estrogens 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.

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 elevated, indicating excessive exposure to this endocrine disrupting chemical (EDC). BPA is derived from plastics and used for manufacturing plastic bottles, wraps for foods, and linings for food cans. BPA leaches from the plastics into beverages and food, which is the main source of exposure.

BPA is very similar to estradiol in that it binds to and activates both membrane and nuclear estrogen receptors, which stimulates growth and proliferation of the prostate.

High BPA levels have been associated with increased risks for many different health issues, including diabetes, breast cancer, and prostate cancer. Researchers have hypothesized that BPA could be metabolized into a mutagenic catechol xenoestrogens, similar to metabolism of estradiol and estrone into 4-catechol estrogens, and contribute to increased risk of developing cancers of the breasts and prostate (Cavalieri E. IUBMB Life 62(10), 746-51, 2010). More recent research has implicated high urinary levels of BPA with increased risk for prostate cancer (Ho SK. Plos One 9[3] e90332, 2014) where it was shown that prostate cancer patients, particularly in men older than 65 years, had much higher levels of creatinine-adjusted BPA (5.47 ug/g Cr) than men without prostate cancer (1.43 ug/g Cr.).

Because urinary BPA is high in this individual who has self-reported prostate cancer, identification of the BPA source and reducing exposure is strongly recommended.

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.

ANDROGENS AND METABOLITES

Testosterone, 5-alpha DHT, and Epi-T are within expected reference ranges for a male. Higher levels of these androgens are expected in younger males who have reached full puberty; levels drop progressively with age; however, this is very individual.

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, which are important for brain and bone health. The most potent of the androgens is dihydrotestosterone (DHT), which is created from testosterone via the enzyme 5a reductase. This enzyme is high in tissues and organs such as the skin, seminal vessicles, prostate, and other organs such as the brain. Testosterone is derived mostly from androstenedione and DHEA. In men most of the testosterone is derived from the testes and a much smaller portion is derived from androstenedione produced by the adrenal glands.

If symptoms of androgen deficiency are, or become, problematic, androgen therapy (DHEA or testosterone) is worth considering, assuming no contraindications.

DHT is the most potent of the androgen metabolites and forms from 5-alpha reductase conversion of T. DHT is formed within cells of target tissues such as the skin and prostate, where it binds to androgen receptors and activates androgen-specific genes. Excessive levels of DHT that can result from overexpression of 5-alpha reductase in the skin can cause conditions such acne and heavier growth of hair on the face and body, but loss of hair on the scalp.

Epi-testosterone (Epi-T) and testosterone (T) are created in about equal amounts from androstenedione. The ratio of T/Epi-T is about 1 under normal circumstances, however this ratio can be much lower in men and women of Asian descent due to deletion polymorphisms in testosterone glucuronidation, which results in less testosterone excreted in urine, but normal levels in serum (Jakobsson J J Clin Endocrinol Metab 91: 687-693, 2006; Strahm E. Br J Sports Med 43: 1126-1130, 2009). Exogenous T therapy usually results in an increase in urinary T, but not Epi-T, the latter of which reflects endogenous T production only. A

T/Epi-T ratio of > 6 is nearly always associated with use of exogenous T, and is used by the Olympic Committee to screen athletes for anabolic steroid use.