P:1300 688 522
E:info@nutripath.com.au
A:PO Box 442 Ashburton VIC3142

Please refer to PDF report attached

Practitioner:	NICOLE CHESTER
	1/39 WAGAWN STREET
	TUGUN QLD
	QLD
	4224
Request id:	4031540
Patient:	HAYLEE MACKEN
	27 PORTOBELLO DRIVE
	MERMAID WATERS QLD
	QLD
	4218
Date of Birth:	20-Jan-1985
Sex:	F

TEST REPORT

 # 2024 10 15 008 U

Ordering Provider:
NutriPath

Samples Received
10/15/2024

Report Date
10/22/2024

Samples Collected
Urine - 10/05/24 06:45
Urine - 10/05/24 09:50
Urine - 10/05/24 16:00
Urine - 10/05/24 20:00

Patient Name: Haylee Macken
Patient Phone Number:

Gender	Last Menses	Height	Waist
Female	09/15/2024	175 cm	130 cm
DOB	**Menses Status**	**Weight**	**BMI**
1/20/1985 (39 yrs)	Pre-Menopausal	127 kg	41.5

TEST NAME	RESULTS | 10/05/24	RANGE
Urinary Estrogens		
Estradiol	1.32	0.78-1.79 µg/g Cr Premeno-luteal or ERT
Estrone	4.14	2.27-5.22 µg/g Cr Premeno-luteal or ERT
Estriol	1.65	0.78-1.98 µg/g Cr Premeno-luteal or ERT
E3/(E1+E2)	0.30	>0.3 (> median value)
2-OH Estradiol	0.36	0.17-0.70 µg/g Cr Premeno-luteal or ERT
2-OH Estrone	2.22	0.70-2.54 µg/g Cr Premeno-luteal or ERT
4-OH Estradiol	0.11	0.10-0.18 µg/g Cr Premeno-luteal or ERT
4-OH Estrone	0.34	0.17-0.47 µg/g Cr Premeno-luteal or ERT
16α-OH Estrone	0.62	0.35-1.07 µg/g Cr Premeno-luteal or ERT
2-OH (E1 + E2)/16-α-OH E1	4.16	1.29-5.49 Premeno-luteal or ERT
2-MeO Estradiol	0.04	0.03-0.08 µg/g Cr Premeno-luteal or ERT
2-MeO Estrone	0.43	0.26-0.68 µg/g Cr Premeno-luteal or ERT
2-MeO E1/2-OH E1	0.19 L	0.21-0.38 Premeno-luteal or ERT
4-MeO Estradiol	0.02	<0.04 µg/g Cr
4-MeO Estrone	0.03	<0.04 µg/g Cr
4-MeO E1/4-OH E1	0.09	0.05-0.13 Premeno-luteal or ERT
4-MeO E2/4-OH E2	0.18	0.10-0.29 Premeno-luteal or ERT
Bisphenol A	<dl L	1.11-3.74 µg/g Cr Premeno-luteal

TEST NAME	RESULTS | 10/05/24	RANGE
Urinary Progestogens		
Pregnanediol	896	465-1609 µg/g Cr Premeno-luteal or PgRT
Allopregnanolone	11.76	2.23-14.87 µg/g Cr Premeno-luteal or PgRT
Allopregnanediol	33.57	14.65-76.71 µg/g Cr Premeno-luteal or PgRT
3α-Dihydroprogesterone	1.22	0.67-2.03 µg/g Cr Premeno-luteal or PgRT
20α-Dihydroprogesterone	10.81	3.93-11.62 µg/g Cr Premeno-luteal or PgRT
Deoxycorticosterone	1.28	0.69-2.23 µg/g Cr Premeno-luteal or PgRT
Corticosterone	4.46	3.19-9.59 µg/g Cr Premeno-luteal or PgRT
Pgdiol/E2	678.79 L	1000-1500 (Optimal Luteal Only)
Urinary Androgens		
DHEA	30.16	15.82-129.17 µg/g Cr Premeno-luteal or DHEAT
Androstenedione	4.06	3.93-13.53 µg/g Cr Premeno-luteal or ART
Androsterone	503	248-937 µg/g Cr Premeno-luteal or ART
Etiocholanolone	699	330-960 µg/g Cr Premeno-luteal or ART
Testosterone	1.36	1.22-3.97 µg/g Cr Premeno-luteal or ART
Epi-Testosterone	3.36	2.01-4.66 µg/g Cr Premeno-luteal
T/Epi-T	0.40 L	0.5-3.0
5α-DHT	1.30	0.28-1.52 µg/g Cr Premeno-luteal or ART
5α,3α-Androstanediol	7.77	2.98-13.10 µg/g Cr Premeno-luteal or ART
Urinary Glucocorticoids		
Total Cortisol	38.80 H	12.26-33.12 µg/g Cr Premeno-luteal
Total Cortisone	76.16 H	23.27-50.88 µg/g Cr Premeno-luteal
Cortisol/Cortisone	0.51	0.5-0.7
Tetrahydrocortisol	601 H	214-546 µg/g Cr Premeno-luteal
Tetrahydrocortisone	1485 H	437-1184 µg/g Cr Premeno-luteal
Urinary Free Diurnal Cortisol		
Free Cortisol	188.11 H	7.8-29.5 µg/g Cr (1st Morning)
Free Cortisol	51.20	23.4-68.9 µg/g Cr (2nd Morning)
Free Cortisol	20.97 H	6.0-19.2 µg/g Cr (Evening)

TEST NAME	RESULTS | 10/05/24	RANGE
Urinary Free Diurnal Cortisol		
Free Cortisol	7.71	2.6-8.4 µg/g Cr (Night)
Urinary Free Diurnal Cortisone		
Free Cortisone	343.12 H	31.6-91.6 µg/g Cr (1st Morning)
Free Cortisone	153.07	63.3-175.8 µg/g Cr (2nd Morning)
Free Cortisone	63.53	30.6-88.5 µg/g Cr (Evening)
Free Cortisone	39.48	15.5-44.7 µg/g Cr (Night)
Urinary Diurnal Melatonin MT6s		
Melatonin	22.59	18.0 - 40.9 µg/g Cr (1st Morning)
Melatonin	5.69 L	7.3 - 31.9 µg/g Cr (2nd Morning)
Melatonin	2.28 H	0.7 - 2.2 µg/g Cr (Evening)
Melatonin	1.15 L	1.7 - 11.1 µg/g Cr (Night)
Urinary Creatinine		
Creatinine (pooled)	1.38	0.3-2.0 mg/mL
Creatinine	0.42	0.3-2.0 mg/mL (1st morning)
Creatinine	1.60	0.3-2.0 mg/mL (2nd morning)
Creatinine	2.07 H	0.3-2.0 mg/mL (Evening)
Creatinine	1.49	0.3-2.0 mg/mL (Night)

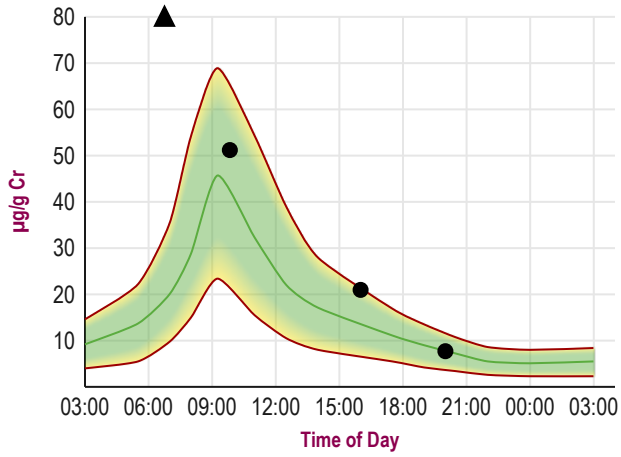
<dl *= Less than the detectable limit of the lab.* ***N/A*** *= Not applicable; 1 or more values used in this calculation is less than the detectable limit.* ***H*** *= High.* ***L*** *= Low.*

Therapies

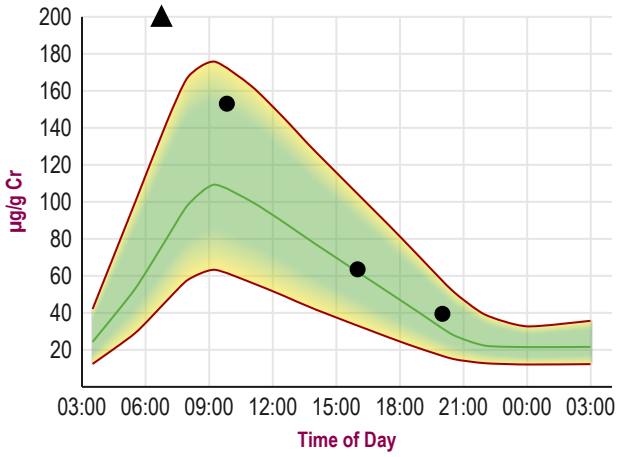
None Indicated

Graphs

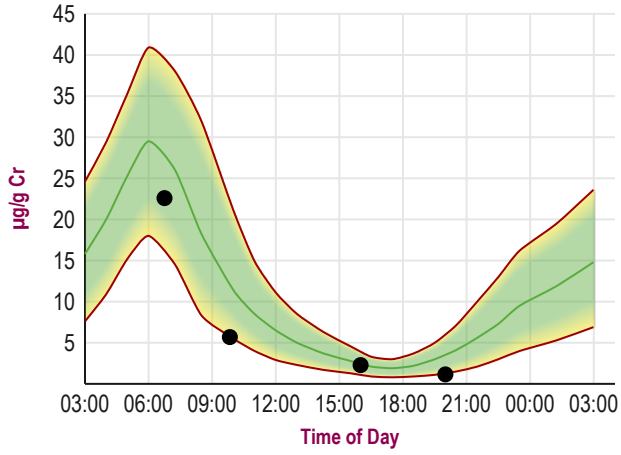
Urinary Free Cortisol



Urinary Free Cortisone



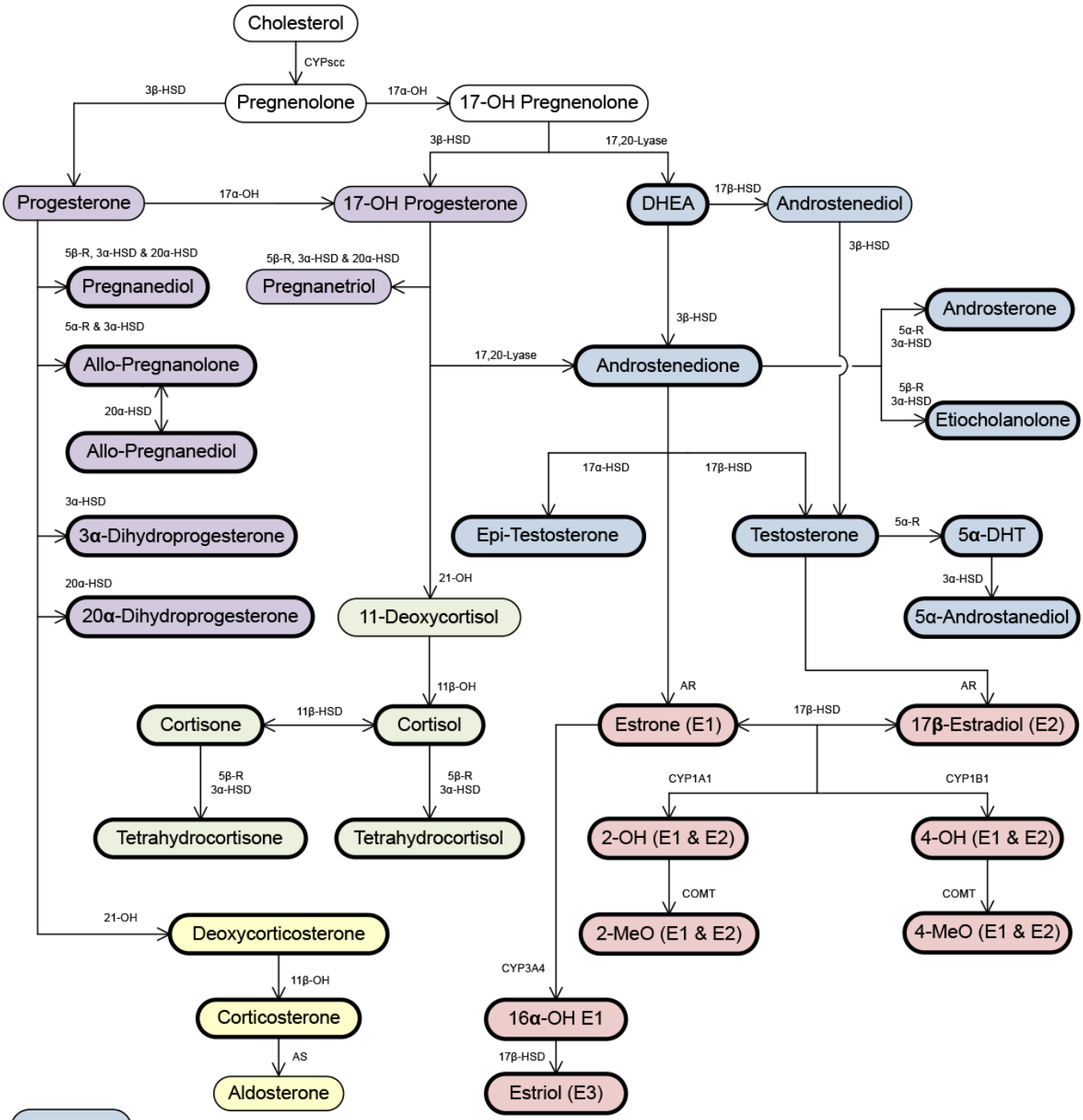
Urinary Melatonin (MT6s)



TEST NAME	WOMEN
Urinary Estrogens	
Estradiol	0.15-0.75 µg/g Cr Postmenopausal; 0.78-1.79 µg/g Cr Premeno-luteal or ERT
Estrone	0.64-2.56 µg/g Cr Postmenopausal; 2.27-5.22 µg/g Cr Premeno-luteal or ERT
Estriol	0.28-1.17 µg/g Cr Postmenopausal; 0.78-1.98 µg/g Cr Premeno-luteal or ERT
E3/(E1+E2)	>0.3 (> median value)
2-OH Estradiol	0.08-0.31 µg/g Cr Postmenopausal; 0.17-0.70 µg/g Cr Premeno-luteal or ERT
2-OH Estrone	0.25-1.00 µg/g Cr Postmenopausal; 0.70-2.54 µg/g Cr Premeno-luteal or ERT
4-OH Estradiol	0.03-0.12 µg/g Cr Postmenopausal; 0.10-0.18 µg/g Cr Premeno-luteal or ERT
4-OH Estrone	0.06-0.22 µg/g Cr Postmenopausal; 0.17-0.47 µg/g Cr Premeno-luteal or ERT
16α-OH Estrone	0.10-0.41 µg/g Cr Postmenopausal; 0.35-1.07 µg/g Cr Premeno-luteal or ERT
2-OH (E1 + E2)/16-α-OH E1	1.47-8.17 Postmenopausal; 1.29-5.49 Premeno-luteal or ERT
2-MeO Estradiol	0.02-0.07 µg/g Cr Postmenopausal; 0.03-0.08 µg/g Cr Premeno-luteal or ERT
2-MeO Estrone	0.06-0.29 µg/g Cr Postmenopausal; 0.26-0.68 µg/g Cr Premeno-luteal or ERT
2-MeO E1/2-OH E1	0.19-0.36 Postmenopausal; 0.21-0.38 Premeno-luteal or ERT
4-MeO Estradiol	<0.04 µg/g Cr
4-MeO Estrone	<0.04 µg/g Cr
4-MeO E1/4-OH E1	0.03-0.38 Postmenopausal; 0.05-0.13 Premeno-luteal or ERT
4-MeO E2/4-OH E2	0.14-0.73 Postmenopausal; 0.10-0.29 Premeno-luteal or ERT
Bisphenol A	1.5-4.5 µg/g Cr Postmenopausal; 1.11-3.74 µg/g Cr Premeno-luteal
Urinary Progestogens	
Pregnanediol	56-220 µg/g Cr Postmenopausal; 465-1609 µg/g Cr Premeno-luteal or PgRT
Allopregnanolone	0.3-1.31 µg/g Cr Postmenopausal; 2.23-14.87 µg/g Cr Premeno-luteal or PgRT
Allopregnanediol	1.38-6.75 µg/g Cr Postmenopausal; 14.65-76.71 µg/g Cr Premeno-luteal or PgRT
3α-Dihydroprogesterone	0.19-0.77 µg/g Cr Postmenopausal; 0.67-2.03 µg/g Cr Premeno-luteal or PgRT
20α-Dihydroprogesterone	0.60-5.53 µg/g Cr Postmenopausal; 3.93-11.62 µg/g Cr Premeno-luteal or PgRT
Deoxycorticosterone	0.37-1.97 µg/g Cr Postmenopausal; 0.69-2.23 µg/g Cr Premeno-luteal or PgRT
Corticosterone	2.32-9.88 µg/g Cr Postmenopausal; 3.19-9.59 µg/g Cr Premeno-luteal or PgRT
Pgdiol/E2	1000-1500 (Optimal Luteal Only)
Urinary Androgens	
DHEA	8.63-37.28 µg/g Cr Postmenopausal; 15.82-129.17 µg/g Cr Premeno-luteal or DHEAT
Androstenedione	2.07-7.94 µg/g Cr Postmenopausal; 3.93-13.53 µg/g Cr Premeno-luteal or ART
Androsterone	152-482 µg/g Cr Postmenopausal; 248-937 µg/g Cr Premeno-luteal or ART
Etiocholanolone	239-777 µg/g Cr Postmenopausal; 330-960 µg/g Cr Premeno-luteal or ART
Testosterone	0.66-2.89 µg/g Cr Postmenopausal; 1.22-3.97 µg/g Cr Premeno-luteal or ART

TEST NAME	WOMEN
Urinary Androgens	
Epi-Testosterone	0.39-1.32 µg/g Cr Postmenopausal; 2.01-4.66 µg/g Cr Premeno-luteal
T/Epi-T	0.5-3.0
5α-DHT	0.26-0.98 µg/g Cr Postmenopausal; 0.28-1.52 µg/g Cr Premeno-luteal or ART
5α,3α-Androstanediol	2.32-8.17 µg/g Cr Postmenopausal; 2.98-13.10 µg/g Cr Premeno-luteal or ART
Urinary Glucocorticoids	
Total Cortisol	13.23-39.26 µg/g Cr Postmenopausal; 12.26-33.12 µg/g Cr Premeno-luteal
Total Cortisone	23.32-59.61 µg/g Cr Postmenopausal; 23.27-50.88 µg/g Cr Premeno-luteal
Cortisol/Cortisone	0.5-0.7
Tetrahydrocortisol	281-711 µg/g Cr Postmenopausal; 214-546 µg/g Cr Premeno-luteal
Tetrahydrocortisone	551-1474 µg/g Cr Postmenopausal; 437-1184 µg/g Cr Premeno-luteal
Urinary Free Diurnal Cortisol	
Free Cortisol	7.8-29.5 µg/g Cr (1st Morning); 23.4-68.9 µg/g Cr (2nd Morning); 6.0-19.2 µg/g Cr (Evening); 2.6-8.4 µg/g Cr (Night)
Urinary Free Diurnal Cortisone	
Free Cortisone	31.6-91.6 µg/g Cr (1st Morning); 63.3-175.8 µg/g Cr (2nd Morning); 30.6-88.5 µg/g Cr (Evening); 15.5-44.7 µg/g Cr (Night)
Urinary Diurnal Melatonin MT6s	
Melatonin	18.0 - 40.9 µg/g Cr (1st Morning); 7.3 - 31.9 µg/g Cr (2nd Morning); 0.7 - 2.2 µg/g Cr (Evening); 1.7 - 11.1 µg/g Cr (Night)
Urinary Creatinine	
Creatinine (pooled)	0.3-2.0 mg/mL
Creatinine	0.3-2.0 mg/mL (1st morning); 0.3-2.0 mg/mL (2nd morning); 0.3-2.0 mg/mL (Evening); 0.3-2.0 mg/mL (Night)

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 | 10/05/24
Estrogen / Progesterone Deficiency	47%
Estrogen Dominance / Progesterone Deficiency	44%
Low Androgens (DHEA/Testosterone)	43%
High Androgens (DHEA/Testosterone)	57%
Low Cortisol	40%
High Cortisol	39%
Hypometabolism	48%
Metabolic Syndrome	40%

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

Lab Comments

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

The parent estrogens are within (or near) the reference ranges seen in premenopausal women. However, symptoms are characteristic of both estrogen excess and deficiency. This suggests that although estrogens were within normal range on the day of testing, they likely fluctuate erratically throughout a 28 day menstrual cycle from high to low, precipitating symptoms of both estrogen deficiency and dominance. This is common in women who are transitioning into menopause when symptoms of both estrogen deficiency (mostly hot flashes and night sweats) and excess are more problematic. When estrogens are within the mid-normal reference intervals, or slightly higher, it is important that they are well balanced with progesterone to prevent excessive proliferation of estrogen sensitive tissues such as the breasts and uterus. Progesterone also helps prevent wide fluctuations in estrogens that occur during the transition to menopause.

If symptoms of estrogen imbalance are problematic (as seen in this individual) consider progesterone restoration therapy as this often helps accelerate estrogen clearance and balance symptoms of both estrogen deficiency and excess. If this is not helpful, consider means to lower the estrogen burden further, or investigate other hormonal imbalances that may be causing symptoms (e.g. low androgens, low or high cortisol, and/or low thyroid).

In the premenopausal patient estradiol should be well balanced with progesterone (optimal PgDiol/E2 ratio = 1300-2000 ug/g Cr during the luteal phase of the menstrual cycle. It is important to note that this optimal ratio only applies to endogenous pregnanediol that is produced during the luteal phase of the menstrual cycle, and not in women treated with exogenous oral, topical or vaginal progesterone. Exogenous oral progesterone results in urinary PgDiol levels higher than range (high Pgdiol/E2 ratio), while topical and vaginal progesterone result in levels lower than range (low Pgdiol/E2 ratio). For a more complete explanation see Progesterone and Metabolites below.

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

The hydroxylated estrogens are within/near expected reference ranges for premenopausal women.

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 quinones.

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 (2-MeO-E2, 2-MeO-E1, 4-MeO-E2, 4-MeO-E1)

The methylated forms of the 2- and 4hydroxyestrogens (2-MeO-E2, 2-MeO-E1, 4-MeO-E2, 4-MeO-E1), are within normal reference ranges or slightly high (beneficial). Adequate methylation of the hydroxyestrogens, and an associated high-normal to 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, 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 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 take a more insidious and dangerous pathway of metabolism, which is oxidation of the hydroxyl (catechol) groups to quinones. Estrogen quinones, especially the 4-quinone of estradiol (4-Quinone-E2) and estrone (4-Quinone-E1) are highly electrophilic and bind to DNA, forming adducts that lead to permanent mutations. Many studies have shown that high urinary levels of these 4-quinones of estradiol and/or estrone are associated with increased breast cancer risk if the 4-hydroxylated estrogens are notinactivated by methylation, or the 4-quine estrogens are inactivated by glutathione sulfation. The 2- and 4-hydroxy estrogens are converted to their more dangerous oxidized quinone forms under oxidizing conditions in the cell, and this occurs more efficiently 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 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 METABOLITES (Pregnanediol-PgDiol, Allopregnanolone-AlloP)

The progesterone metabolites, pregnanediol (PgDiol) and allopregnanolone (AlloP), are within expected reference ranges for premenopausal women. PgDiol is a metabolite and surrogate marker of serum progesterone. AlloP is another progesterone metabolite that freely enters the brain from the bloodstream through the blood brain barrier and serves as a neuroactive steroid. AlloP binds to GABAa receptors in the brain and has a calming (anxiolytic) and sleep-inducing effect at high concentrations. Only high levels of AlloP, achieved at peak of an optimal luteal phase, during pregnancy, and with progesterone therapy, have the anxiolytic effects on GABAa receptors in the brain. In a small percentage (about

5-10%) of premenopausal women AlloP at physiological levels has a paradoxical effect and causes anxiety (anxiogenic) and other symptoms characteristic of premenstrual dysphoric disorder (PMDD). This is thought to be due to individual differences in the subunit structure of GABAa receptors in the brain.

PROGESTERONE METABOLITES

The urinary progesterone metabolites are within, or near, normal reference ranges seen in premenopausal women. The urinary progestogen metabolites included encompass the primary urinary metabolite, pregnanediol (Pgdiol), and four other more minor metabolites that belong to the pregnane (Allo-pregnanolone, Allo-pregnanediol) and pregnene (3a-dihydroprogesterone, 20a-dihydroprogesterone) categories. In postmenopausal women the level of pregnanediol is expected to be much lower than in premenopausal women (mean values 81 and 1324 µg/g creatinine, respectively). The mean and range levels for urinary pregnanediol established in premenopausal women during the early follicular and mid-luteal phases of the menstrual cycle are 152 µg/g creatinine (range 92-346) and 1324 µg/g creatinine (range 579-1700), respectively. Thus, about a 10-fold increase in Pgdiol is expected during the progression from the follicular to the luteal phase of the menstrual cycle. The urinary ranges of pregnanediol during the luteal phase are equivalent to a range of about 3-25 ng/mL progesterone in blood (capillary whole blood, venous serum or plasma) and about 50-250 pg/mL in saliva. Optimal luteal ovarian production of progesterone is reflected in all three body fluids (urine, blood, salivary), which is roughly > 1300 µg PgDiol/g creatinine in urine, > 10 ng Progesterone/mL in blood, and > 100 pg Progesterone/mL in saliva.

While the level of urinary pregnanediol is optimal for a premenopausal woman, the ratio of pregnanediol to estrradiol (PgDiol/E2) is low, indicating an overall dominance of estradiol relative to progesterone. This occurs commonly in women approaching menopause (perimenopause) from about age 45-55, and is associated with symptoms of both estrogen dominance and deficiency, as the estrogen levels fluctuate erratically from high to low throughout a menstrual cycle. Progesterone therapy is often helful as it helps reduce the estrogen burden and desensitizes estrogen sensitive tissues such as the breasts and uterus by down-regulating estrogen receptors. However, when estradiol is too excessive progesterone is less effective and other means to lower the estrogen burden should be considered before using progesterone.

PROGESTERONE METABOLITES: MINERALCORTICOID PRECURSORS

Deoxycorticosterone (DOC) and cortiscosterone (CC) are within/near the expected reference ranges for a premenopausal woman. DOC and CC are downstream metabolites of progesterone and progesterone therapy, particularly oral progesterone, usually increases DOC and CC beyond reference ranges.

DOC is a weak mineralcorticoid and precursor to the more potent mineralcorticoid aldosterone. The conversion of progesterone to DOC varies by up to 20-fold among women (MacDonald Endocrine Reviews 12: 372-401, 1991) p. 390). Adverse reactions to higher progesterone that occur during the luteal phase of the menstrual cycle, pregnancy, or with progesterone replacement therapy may involve high conversion to DOC.

ANDROGEN PRECURSOR (DHEA/S)

Total urinary DHEA(S) and its downstream hormone androstenedione are within normal reference ranges. DHEA is synthesized in the adrenal glands and is rapidly sulfated to DHEA-sulfate (DHEAS) to extend its half-life in blood. DHEA is converted to androstenedione and then to 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 considered a universal precursor to both androgens (androstenedione, testosterone, DHT), and estrogens (estradiol and estrone). DHEA is commonly used as a supplement to raise both DHEA and testosterone levels in women. Much less DHEA is converted to T and DHT in men.

DHEA itself has very little androgenic activity and serves mostly as a precursor to other downstream more potent metabolites (androgens and estrogens). In the sulfated form DHEA sulfate (DHEAS) plays an important role in the integrity of the immune system via binding to specific DHEAS binding sites on lymphocytes. In the brain DHEAS acts as a neuroactive steroid where it modifies dopaminergic pathways responsible for uplifting mood and increasing feeling of wellbeing.

DHEA METABOLITES: (ANDROSTERONE, ETIOCHOLANOLONE)

Etiocholanolone and androsterone are within expected reference ranges. These hormones are downstream metabolites of DHEA and androstenedione (see Steroid Hormone Cascade). As a precursor molecule, DHEA is metabolized to androstenedione, which is then converted to etiocholanolone or androsterone through 5-beta or 5-alpha reductase enzymes, respectively. Androsterone, because it is created from the same enzyme (5 alpha reductase) that converts testosterone to dihydrotestosterone, provides a good secondary marker of 5 alpha reductase activity. This enzyme also converts progesterone to 5 alpha dihydroprogesterone (5a-DHP), a precursor to the neuroactive steroid allopregnanolone (5 alpha, 3 alpha tetrahydroprogesterone). Higher levels of etiocholanolone are believed to lower cancer risk by inhibiting glucose utilization, essential for tumor growth.

ANDROGENS AND METABOLITES

Testosterone, 5-alpha DHT, and Epi-T are within expected ranges for a premenopausal woman. If symptoms of androgen deficiency are, or

become, problematic, androgen therapy (DHEA or testosterone) is worth considering, assuming no contraindications. DHEA therapy increases both DHEAS and testosterone levels in women, but may also increase estrogens, which need to be countered with natural progesterone if increased by DHEA.

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. Following menopause the ovarian contribution of androgens is lower.

EPI-TESTOSTERONE AND RELATIONSHIP TO TESTOSTERONE.

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. When testosterone is supplemented with any delivery system except topical, the T/Epi-T ratio increases, which reflects an increase in the exogenous testosterone, but not Epi-T, which represents endogenous production.

5-ALPHA 3-ALPHA ANDROSTANEDIOL (ADIOL)

The downstream metabolite of DHT, 5-alpha 3-alpha androstanediol (Adiol), is within expected reference range. Adiol is considered a neuroactive steroid that can passively enter the brain from the bloodstream through the blood brain barrier.

Adiol binds to GABAa receptors in the brain and has a similar anxiolytic (calming) effect, albeit weaker than allopregnanolone. It also interacts with the dopaminergic pathways in the brain and is associated with the dopamine pleasure and reward pathway. Thus, low levels of Adiol are more likely to be associated with conditions/symptoms common to low dopamine, and high levels with high dopamine. Fibromyalgia and chronic fatigue syndrome (CFS) are common in individuals with low dopamine, as are symptoms of brain fog, achy muscles, and excessive fatigue.

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 CORTISONE (E)

Urinary free cortisol (F) and its inert metabolite cortisone (E) are following a normal circadian rhythm and within expected reference ranges with exception of the high F and E in the first morning void.

Excessive stressors that occur In the early hours of the morning before waking may cause the first morning cortisol and cortisone to rise above the reference range, as seen in these results. If the adrenals are healthy and the stressor acute the cortisol should progressively drop in the evening and night voids and remain within normal reference range. If the stressor persists, and the adrenal glands are healthy, cortisol levels will usually remain above the reference range throughout the remainder of the day and before bed at night.

The most common stressors that can raise F and E levels and can eventually cause adrenal exhaustion and low cortisol 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). While acute stressors such as exercise are expected to raise cortisol levels over the interval of the stressor, chronic and persistent stressors can eventually lead to adrenal exhaustion (insufficiency) and low cortisol. Adequate rest, avoiding stressors as much as possible, and supplementation with nutrients that support adrenal gland function and cortisol synthesis are often helpful (e.g. eating a higher protein rich diet, use of natural progesterone-a cortisol precursor, supplementation with vitamins and minerals that support adrenal cortisol synthesis, etc.)

A normal daily output of cortisol is essential to maintain normal metabolic activity, help regulate steady state glucose levels (important for brain function and energy production), and optimize immune function. However, high and persistent cortisol can have opposite effects on these functions. 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; "The Role of Stress and the HPA Axis in Chronic Disease Management" by Thomas Guilliams, PhD.

MELATONIN METABOLITE 6-SULFATOXYMELATONIN (MT6s)

The melatonin metabolite MT6s is low to low-normal (flatter pattern) throughout most of the day, and not showing a normal circadian rhythm. Low melatonin can contribute to sleep problems. If sleep is problematic and melatonin supplementation is not helpful, 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.

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