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

Please refer to PDF report attached

Practitioner:	RACHEAL LEE (NPINS) SHOP 6/115 SHINGLEY DRIVE AIRLIE BEACH QLD QLD 4802
Request id:	4048155
Patient:	KARLA POUND 1/75 COUNTRY ROAD CANNONVALE QLD QLD 4802
Date of Birth:	22-Jul-1988
Sex:	F

TEST REPORT

NutriPATH

 # 2024 12 03 086 U

Ordering Provider:
NutriPath

Samples Received
12/03/2024

Report Date
12/11/2024

Samples Collected
Urine - 11/21/24 05:00
Urine - 11/21/24 07:00
Urine - 11/21/24 16:00
Urine - 11/21/24 20:00

Patient Name: Karla Pound
Patient Phone Number:

Gender	Last Menses	Height	Waist
Female	Unspecified	Unspecified	Unspecified
DOB	**Menses Status**	**Weight**	
7/22/1988 (36 yrs)	Pre-Menopausal	Unspecified	

TEST NAME	RESULTS | 11/21/24	RANGE
Urinary Estrogens		
Estradiol	0.49 L	0.78-1.79 µg/g Cr Premeno-luteal or ERT
Estrone	1.13 L	2.27-5.22 µg/g Cr Premeno-luteal or ERT
Estriol	0.45 L	0.78-1.98 µg/g Cr Premeno-luteal or ERT
E3/(E1+E2)	0.28 L	>0.3 (> median value)
2-OH Estradiol	0.38	0.17-0.70 µg/g Cr Premeno-luteal or ERT
2-OH Estrone	1.13	0.70-2.54 µg/g Cr Premeno-luteal or ERT
4-OH Estradiol	0.07 L	0.10-0.18 µg/g Cr Premeno-luteal or ERT
4-OH Estrone	0.16 L	0.17-0.47 µg/g Cr Premeno-luteal or ERT
16α-OH Estrone	0.18 L	0.35-1.07 µg/g Cr Premeno-luteal or ERT
2-OH (E1 + E2)/16-α-OH E1	8.39 H	1.29-5.49 Premeno-luteal or ERT
2-MeO Estradiol	0.03	0.03-0.08 µg/g Cr Premeno-luteal or ERT
2-MeO Estrone	0.16 L	0.26-0.68 µg/g Cr Premeno-luteal or ERT
2-MeO E1/2-OH E1	0.14 L	0.21-0.38 Premeno-luteal or ERT
4-MeO Estradiol	<dl L	<0.04 µg/g Cr
4-MeO Estrone	0.02	<0.04 µg/g Cr
4-MeO E1/4-OH E1	0.13	0.05-0.13 Premeno-luteal or ERT
4-MeO E2/4-OH E2	N/A	0.10-0.29 Premeno-luteal or ERT
Bisphenol A	<dl L	1.11-3.74 µg/g Cr Premeno-luteal

TEST NAME	RESULTS | 11/21/24	RANGE
Urinary Progestogens		
Pregnanediol	1165	465-1609 µg/g Cr Premeno-luteal or PgRT
Allopregnanolone	26.93 H	2.23-14.87 µg/g Cr Premeno-luteal or PgRT
Allopregnanediol	53.62	14.65-76.71 µg/g Cr Premeno-luteal or PgRT
3α-Dihydroprogesterone	3.01 H	0.67-2.03 µg/g Cr Premeno-luteal or PgRT
20α-Dihydroprogesterone	7.29	3.93-11.62 µg/g Cr Premeno-luteal or PgRT
Deoxycorticosterone	1.23	0.69-2.23 µg/g Cr Premeno-luteal or PgRT
Corticosterone	7.62	3.19-9.59 µg/g Cr Premeno-luteal or PgRT
Pgdiol/E2	2377.55 H	1000-1500 (Optimal Luteal Only)
Urinary Androgens		
DHEA	7.68 L	15.82-129.17 µg/g Cr Premeno-luteal or DHEAT
Androstenedione	3.42 L	3.93-13.53 µg/g Cr Premeno-luteal or ART
Androsterone	496	248-937 µg/g Cr Premeno-luteal or ART
Etiocholanolone	378	330-960 µg/g Cr Premeno-luteal or ART
Testosterone	1.52	1.22-3.97 µg/g Cr Premeno-luteal or ART
Epi-Testosterone	2.00 L	2.01-4.66 µg/g Cr Premeno-luteal
T/Epi-T	0.76	0.5-3.0
5α-DHT	0.42	0.28-1.52 µg/g Cr Premeno-luteal or ART
5α,3α-Androstanediol	4.06	2.98-13.10 µg/g Cr Premeno-luteal or ART
Urinary Glucocorticoids		
Total Cortisol	21.36	12.26-33.12 µg/g Cr Premeno-luteal
Total Cortisone	52.63 H	23.27-50.88 µg/g Cr Premeno-luteal
Cortisol/Cortisone	0.41 L	0.5-0.7
Tetrahydrocortisol	277	214-546 µg/g Cr Premeno-luteal
Tetrahydrocortisone	523	437-1184 µg/g Cr Premeno-luteal
Urinary Free Diurnal Cortisol		
Free Cortisol	13.23	7.8-29.5 µg/g Cr (1st Morning)
Free Cortisol	31.03	23.4-68.9 µg/g Cr (2nd Morning)
Free Cortisol	14.50	6.0-19.2 µg/g Cr (Evening)

TEST NAME	RESULTS | 11/21/24	RANGE
Urinary Free Diurnal Cortisol		
Free Cortisol	<dl L	2.6-8.4 µg/g Cr (Night)
Urinary Free Diurnal Cortisone		
Free Cortisone	43.32	31.6-91.6 µg/g Cr (1st Morning)
Free Cortisone	222.22 H	63.3-175.8 µg/g Cr (2nd Morning)
Free Cortisone	64.61	30.6-88.5 µg/g Cr (Evening)
Free Cortisone	38.18	15.5-44.7 µg/g Cr (Night)
Urinary Diurnal Melatonin MT6s		
Melatonin	29.59	18.0 - 40.9 µg/g Cr (1st Morning)
Melatonin	10.90	7.3 - 31.9 µg/g Cr (2nd Morning)
Melatonin	0.91	0.7 - 2.2 µg/g Cr (Evening)
Melatonin	<dl L	1.7 - 11.1 µg/g Cr (Night)
Urinary Creatinine		
Creatinine (pooled)	1.21	0.3-2.0 mg/mL
Creatinine	1.92	0.3-2.0 mg/mL (1st morning)
Creatinine	0.66	0.3-2.0 mg/mL (2nd morning)
Creatinine	1.65	0.3-2.0 mg/mL (Evening)
Creatinine	0.19 L	0.3-2.0 mg/mL (Night)

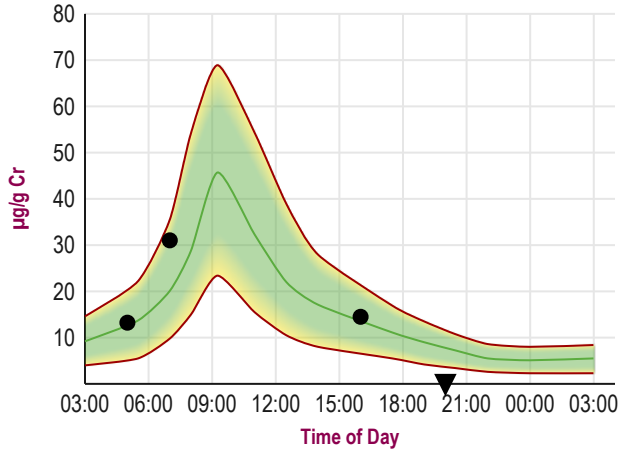
<dl *= Less than the detectable limit of the lab.* ***N/A*** *= Not applicable; 1 or more values used in this calculation is less than the detectable limit.* ***H*** *= High.* ***L*** *= Low.*

Therapies

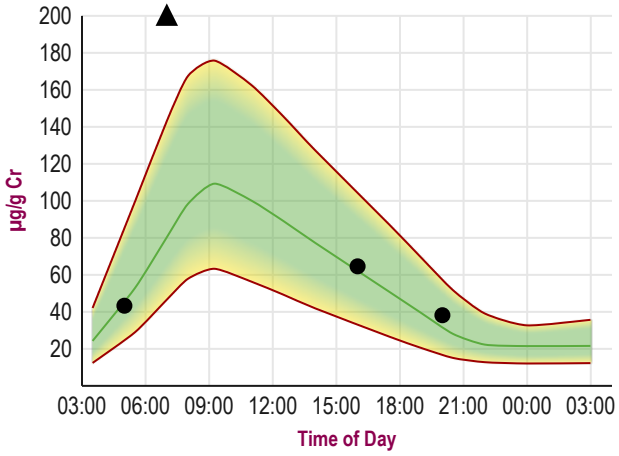
None Indicated

Graphs

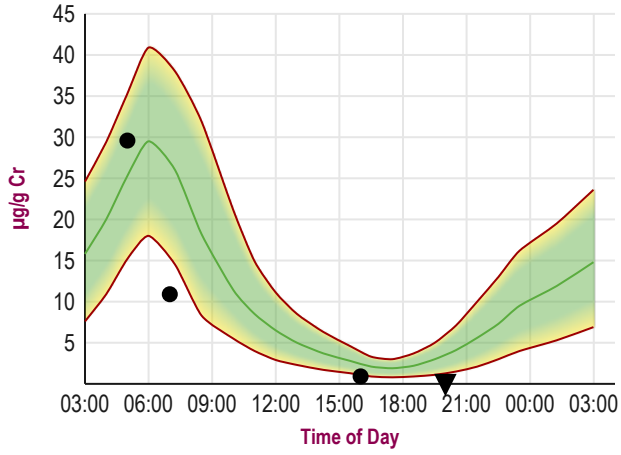
Urinary Free Cortisol



Urinary Free Cortisone



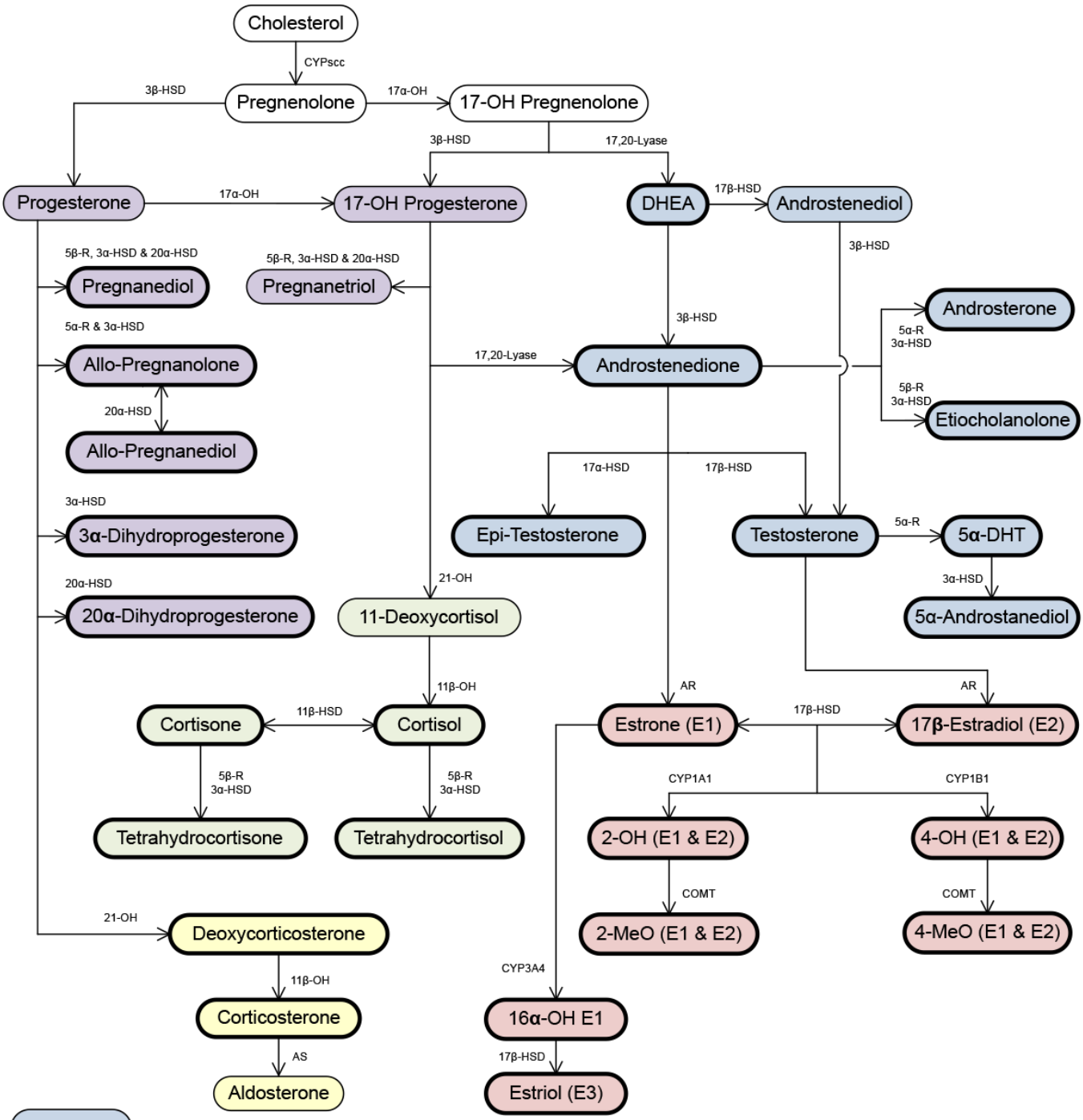
Urinary Melatonin (MT6s)



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

Lab Comments

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

The parent estrogens are low or within the lower quadrant of the reference ranges seen in premenopausal women. Assuming urine was collected during luteal phase of the menstrual cycle, low estrogens usually results from anovulation or use of contraceptives that contain synthetic hormones (e.g. ethinyl estradiol) that suppress endogenous estrogen synthesis by the ovaries (none indicated). When estrogens are low over a prolonged period of time this is usually associated with estrogen deficiency symptoms (e.g. hot flashes, night sweats, vaginal dryness, sleep disturbances, etc.); however, if a synthetic estrogen like ethinyl is present it will not be detectable, endogenous estradiol will be low (suppressed), but symptoms of estrogen deficiency will be minimal since ethinyl estradiol is a potent estrogen at the tissue level. Adequate estrogen is necessary for maintaining healthy skin, bones, nerves (raises pain threshold) and brain function (helps create neurotransmitters), and in concert with progesterone helps maintain optimal tissue sensitivity to insulin (prevents insulin resistance).

HYDROXYLATED ESTROGENS (2-OH E2 & E1, 4-OH E2 & E1, 16-OH E1)

The 2-hydroxylated (catechol) estrogens (2-OH-E2 and 2-OH-E1) are within reference ranges, whereas the 4-hydroxylated estrogens (4-OH-E2 and 4-OH-E1) are lower than reference ranges (considered beneficial).

The 2-hydroxylated estrogens are considered a safer form of catechol estrogens because their down-stream 2-quinone estrogens are not mutagenic. In contrast, the 4-hydroxylated estrogens, when they are oxidized further to 4-quinone estrogens are very mutagenic, damage DNA, and increase risk for cancer. Thus, higher levels of 2-hydroxyestrogens relative to 4-hydroxyestrogens should be considered as beneficial and carry a lower lifetime risk for development of breast cancer. Any increase in 4-OH-E2 or 4-OH-E1 beyond reference ranges should be considered as a potentially higher risk for breast cancer, especially if they are not neutralized by methylation (see below-methylation of 4-hydroxyestrogens).

The hydroxylation of estradiol and estrone at the 2, 4, or 16 positions on E2 and E1 represents the first phase of metabolism and elimination of these estrogens via urine. Following hydroxylation the estrogens undergo further Phase 2 modification (methylation, sulfation, glucuronidation) that inactivates them (eliminates their estrogenic potential and prevents them from further oxidizing to more toxic estrogen quinones) and increases their solubility and excretion in urine and bile/feces.

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), the latter of 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). Therefore, maintaining low estrogen hydroxylation, or increasing 2-hydroxylation relative to 4-hydroxylation, should be considered as a long-term strategy to prevent damage to breast epithelial cells that could potentially lead to breast cancer.

The safer 2-hydroxylated estrogen metabolism is increased by consumption of cruciferous vegetables and/or extracts of them. The most commonly used extracts 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. Heavy metals, via the creation of excessive Reactive Oxygen Species (ROS) in tissues accelerate oxidation of 4-catechol estrogens to 4-quinones; therefore, means to reduce heavy metal exposure, should it be problematic, or preventing heavy metal stimulation of ROS with antioxidants or essential elements (e.g. selenium) should help reduce formation of toxic and mutagenic 4-estrogen quinones.

16-OH-E1 is a precursor to estriol (see Steroid Hormone Cascade). Early clinical research 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-OH-E1 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-hydroxyestrogens (2-MeO-E2, 2-MeO-E1) and 4-hydroxyestrogens (4-MeO-E2, 4-MeO-E1) are low or lower than the median of the reference ranges. When the hydroxyestrogens are within range or higher this indicates poor methylation. This is also apparent from the low 4-MeO-E2/4-OH-E2 ratio. Increased urinary levels of the 4-hydroxyestrogens (4-OH-E2 and 4-OH-E1), in the absence of their methylation, are associated with increased risk for cancers of reproductive tissues such as breasts and uterus in females and prostate in males.

The 2- and 4- hydroxyl estrogens are methylated by the enzyme Catechol-o-Methyl Transferase (COMT), which renders them inert (Cavalieri EL, Rogan EG Future Oncol 6(1): 75-79, 2010). In this form the methylated catechol estrogens are rapidly excreted in urine. When methylation of catechol estrogens is inadequate, due to low levels of COMT, or lack of precursors of methylation (i.e. vitamins B6, B12, folate, betaine), the 2- and 4-hydroxylestrogens can further oxidize to more highly reactive 2- or 4-estrogen quinones. The 4-quinones of estradiol and estrone,

formed from 4-OH-E2 and 4-OH-E1, are highly electrophilic and bind to DNA forming adducts that lead to permanent mutations in the DNA. The 2-quinones of estradiol and estrone, formed from 2-OH-E2 and 2-OH-E1, will also form covalent adducts with DNA, but this is repaired without DNA damage (mutations).

Formation of 2- and 4-estrogen quinones occurs more readily in the presence of oxidized lipids such as trans-hydrogenated fats, heavy metals, and other conditions that enhance reactive oxygen species (ROS) in tissues. Estrogen quinones are inactivated by many different types of sulfur- or selenium-containing antioxidants, such as N-acetyl cysteine, glutathione, and glutathione peroxidase. Glutathione, the most ubiquitous antioxidant in the body, binds to and inactivates estrogen quinones; therefore, means to maintain high levels of this antioxidant are key to preventing estrogen quinones, as well as other ROS from causing DNA mutations that potentially can lead to cancer. 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).

Consider means to reduce the estrogen burden (e.g. lower therapies that increase estrogen levels-e.g. estrogen replacement therapies in women and testosterone therapies in men) and consider diets that will help with estrogen clearance (lower consumption of meats and increase vegetables with color and fiber). Consumption of vitamins that decrease ROS (all forms of antioxidants) and increase methylation (e.g. folate, B6, B12, betaine) may also be helpful.

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 metabolite pregnanediol (PgDiol) is within expected reference range for a premenopausal women. PgDiol is a metabolite and surrogate marker of serum progesterone; PgDiol in urine rises in parallel with levels of Pg in blood and saliva of premenopausal women during the luteal phase of the menstrual cycle. If the PgDiol/E2 ratio is low this usually indicates luteal insufficiency. Consider progesterone therapy if PgDiol/E2 is low, and symptoms of estrogen dominance are problematic.

In contrast to normal levels of PgDiol, the neuroactive progesterone metabolite allopregnanolone (AlloP) is higher than reference range. This suggests that the level/activity of enzyme 5-alpha reductase is high as this enzyme converts progesterone to 5-hydroxyprogesterone (5-HP) which is then converted to AlloP by the enzyme 3 alpha hydroxysteroid dehydrogenase (see Steroid Hormone Cascade). High levels of AlloP are often associated with high levels of other steroids that are metabolized by 5-alpha reductase (e.g. testosterone to dihydrotestosterone).

AlloP is a potent neuroactive steroid that freely enters the brain from the bloodstream through the blood brain barrier where it binds to GABAa receptors in neurons inducing a calming (anxiolytic) and sleep-inducing effect. 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).

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 PRECURSORS (ANDROSTENEDIOL, DHEA)

The androgen precursors, androstenedione and DHEA, are lower than normal reference ranges for a premenopausal woman.

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 the estrogen, estrone, occurs in individuals with higher amounts of adipose (fat) tissue.

Consider DHEA supplementation if low androgen symptoms are problematic. DHEA is an androstenedione precursor and is commonly used as a supplement to raise testosterone levels in women.

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 (T), its epimer, Epi-testosterone (Epi-T), and its more potent metabolite, 5-alpha DHT (DHT) are low or lower than the median reference range for a premenopausal woman, suggesting androgen deficiency. 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.

During the premenopausal years about half of the testosterone is derived from the ovaries, and the remainder from the adrenal glands via DHEA and androstenedione. At menopause most of the T is derived from the adrenal glands. If the adrenal precursor to testosterone, DHEA/S, is low this can result in low T. In women, DHEA therapy can raise levels of both DHEA and T. When aromatase is adequate the DHEA and T will also raise levels of estrone and estradiol, respectively. Since both T and DHEA are low, consider DHEA therapy.

The T precursors (see Steroid Hormone Cascade), DHEA and androstenedione, are also low or low-normal, suggesting adrenal fatigue may contribute to the overall low level of androgens.

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.

Low androgens, particularly the more potent androgens testosterone and DHT, are associated with many different adverse conditions (bone loss, thinning skin, vaginal dryness, incontinence, cardiovascular disease, insulin resistance/metabolic syndrome, breast cancer) and symptoms (fatigue, low stamina, depression, memory lapses, loss of sex drive, hot flashes, allergies). Because these androgens are all low consider supplementing with DHEA or testosterone. Androgen therapy also helps to increase estrogen levels as androgens are precursors to estrogens (estradiol and estrone).

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 (F, E, THF, THE)

Total cortisol (F) and cortisone (E), and their down-stream metabolites, tetrahydrocortisol (THF) and tetrahydrocortisone (THE), are within/near the normal reference ranges.

The total levels of these four glucocorticoids are determined from the average of four urine collections throughout the day and are very similar to the 24-hour urine values. To appreciate baseline and supplemented cortisol levels it is more appropriate to test cortisol levels throughout the day (following cortisol therapy) by the urinary free cortisol test (see below).

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, free cortisone (E) are within/near expected reference ranges throughout the day and are following a normal circadian rhythm. Symptoms were NOT reported; therefore, comments relating symptoms to test results are not possible.

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. When cortisol levels are within normal range under situations of excessive stress, as reported herein, this usually indicates that the adrenal glands are overworking to keep up with the demands of the stress(ors). These conditions are most commonly caused by one or more of the following: psychological stress (emotional), physical insults (surgery, injury), diseases (cancer, diabetes), chemical exposure (environmental pollutants, excessive medications), and/or pathogenic infections (bacteria, viruses and fungi).

When these stressors persist, or become worse, over time this can lead to adrenal exhaustion, low cortisol levels, and symptoms which often overlap with those of high cortisol (e.g. fatigue, sleep disturbances, low thyroid symptoms) or are more characteristic only of low cortisol (e.g. allergies-immune dysfunction, chemical sensitivity, and sugar craving due to hypoglycemia). For additional information about strategies to support adrenal health and reduce stress(ors) that can lead to high or low cortisol, the following books are worth reading: "Adrenal Fatigue; The 21st Century Stress Syndrome", 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 urine melatonin metabolite MTGs is within normal reference ranges in the first morning, second morning, and evening voids, but drops thereafter to a level lower than reference range. This pattern could occur with excessive lighting at night, which suppresses melatonin synthesis. Consider melatonin supplementation if no contraindication (see: http://www.nlm.nih.gov/medlineplus/druginfo/natural/940.html

Melatonin, produced by the pineal gland in the brain, is released into the circulation where it rapidly enters tissues throughout the body. 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. Low night time melatonin levels are seen in breast and prostate cancer patients.

Because of its established role in the regulation of the circadian rhythm, 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.