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)<br>SHOP 6/115 SHINGLEY DRIVE<br>AIRLIE BEACH QLD<br>QLD<br>4802 |
| **Request id:** | 4088621 |
| **Patient:** | ALICE COPPING<br>27 SOUTH MOLLE BOULEVARD<br>CANNONVALE QLD<br>QLD<br>4802 |
| **Date of Birth:** | 14-Jan-1994 |
| **Sex:** | F |

# TEST REPORT

**# 2025 04 15 024 U**

**Ordering Provider:**
NutriPath

**Samples Received**
04/15/2025

**Report Date**
04/21/2025

**Samples Collected**
Urine - 03/31/25 05:30
Urine - 03/31/25 07:45
Urine - 03/31/25 17:35
Urine - 03/31/25 20:13

**Patient Name:** Alice Copping
**Patient Phone Number:**

| Gender | Last Menses | Height | Waist |
|---|---|---|---|
| Female | 03/11/2025 | 164 cm | Unspecified |
| **DOB** | **Menses Status** | **Weight** | **BMI** |
| 1/14/1994 (31 yrs) | Pre-Menopausal - Irregular | 69 kg | 25.7 |

| TEST NAME | RESULTS \| 03/31/25 | RANGE |
|---|---|---|
| **Urinary Estrogens** | | |
| **Estradiol** | 1.44 | 0.78-1.79 µg/g Cr Premeno-luteal or ERT |
| **Estrone** | 3.01 | 2.27-5.22 µg/g Cr Premeno-luteal or ERT |
| **Estriol** | 0.50 L | 0.78-1.98 µg/g Cr Premeno-luteal or ERT |
| **E3/(E1+E2)** | 0.11 L | >0.3 (> median value) |
| **2-OH Estradiol** | 0.60 | 0.17-0.70 µg/g Cr Premeno-luteal or ERT |
| **2-OH Estrone** | 1.93 | 0.70-2.54 µg/g Cr Premeno-luteal or ERT |
| **4-OH Estradiol** | 0.13 | 0.10-0.18 µg/g Cr Premeno-luteal or ERT |
| **4-OH Estrone** | 0.26 | 0.17-0.47 µg/g Cr Premeno-luteal or ERT |
| **16α-OH Estrone** | 0.32 L | 0.35-1.07 µg/g Cr Premeno-luteal or ERT |
| **2-OH (E1 + E2)/16-α-OH E1** | 7.91 H | 1.29-5.49 Premeno-luteal or ERT |
| **2-MeO Estradiol** | 0.05 | 0.03-0.08 µg/g Cr Premeno-luteal or ERT |
| **2-MeO Estrone** | 0.33 | 0.26-0.68 µg/g Cr Premeno-luteal or ERT |
| **2-MeO E1/2-OH E1** | 0.17 L | 0.21-0.38 Premeno-luteal or ERT |
| **4-MeO Estradiol** | <dl L | <0.04 µg/g Cr |
| **4-MeO Estrone** | 0.01 | <0.04 µg/g Cr |
| **4-MeO E1/4-OH E1** | 0.04 L | 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** | 0.88 L | 1.11-3.74 µg/g Cr Premeno-luteal |

| TEST NAME | RESULTS \| 03/31/25 | RANGE |
|---|---|---|
| **Urinary Progestogens** | | |
| Pregnanediol | 1115 | 465-1609 µg/g Cr Premeno-luteal or PgRT |
| Allopregnanolone | 14.16 | 2.23-14.87 µg/g Cr Premeno-luteal or PgRT |
| Allopregnanediol | 64.75 | 14.65-76.71 µg/g Cr Premeno-luteal or PgRT |
| 3α-Dihydroprogesterone | 2.85 H | 0.67-2.03 µg/g Cr Premeno-luteal or PgRT |
| 20α-Dihydroprogesterone | 8.46 | 3.93-11.62 µg/g Cr Premeno-luteal or PgRT |
| Deoxycorticosterone | 0.78 | 0.69-2.23 µg/g Cr Premeno-luteal or PgRT |
| Corticosterone | 2.94 L | 3.19-9.59 µg/g Cr Premeno-luteal or PgRT |
| Pgdiol/E2 | 774.31 L | 1000-1500 (Optimal Luteal Only) |
| **Urinary Androgens** | | |
| DHEA | 51.34 | 15.82-129.17 µg/g Cr Premeno-luteal or DHEAT |
| Androstenedione | 10.14 | 3.93-13.53 µg/g Cr Premeno-luteal or ART |
| Androsterone | 919 | 248-937 µg/g Cr Premeno-luteal or ART |
| Etiocholanolone | 622 | 330-960 µg/g Cr Premeno-luteal or ART |
| Testosterone | 4.72 H | 1.22-3.97 µg/g Cr Premeno-luteal or ART |
| Epi-Testosterone | 4.70 H | 2.01-4.66 µg/g Cr Premeno-luteal |
| T/Epi-T | 1.00 | 0.5-3.0 |
| 5α-DHT | 1.50 | 0.28-1.52 µg/g Cr Premeno-luteal or ART |
| 5α,3α-Androstanediol | 16.00 H | 2.98-13.10 µg/g Cr Premeno-luteal or ART |
| **Urinary Glucocorticoids** | | |
| Total Cortisol | 10.72 L | 12.26-33.12 µg/g Cr Premeno-luteal |
| Total Cortisone | 28.35 | 23.27-50.88 µg/g Cr Premeno-luteal |
| Cortisol/Cortisone | 0.38 L | 0.5-0.7 |
| Tetrahydrocortisol | 265 | 214-546 µg/g Cr Premeno-luteal |
| Tetrahydrocortisone | 475 | 437-1184 µg/g Cr Premeno-luteal |
| **Urinary Free Diurnal Cortisol** | | |
| Free Cortisol | 7.80 | 7.8-29.5 µg/g Cr (1st Morning) |
| Free Cortisol | 13.39 L | 23.4-68.9 µg/g Cr (2nd Morning) |
| Free Cortisol | 2.72 L | 6.0-19.2 µg/g Cr (Evening) |

| TEST NAME | RESULTS \| 03/31/25 | RANGE |
|---|---|---|
| **Urinary Free Diurnal Cortisol** | | |
| **Free Cortisol** | 2.23 L | 2.6-8.4 µg/g Cr (Night) |
| **Urinary Free Diurnal Cortisone** | | |
| **Free Cortisone** | 44.23 | 31.6-91.6 µg/g Cr (1st Morning) |
| **Free Cortisone** | 75.03 | 63.3-175.8 µg/g Cr (2nd Morning) |
| **Free Cortisone** | 32.55 | 30.6-88.5 µg/g Cr (Evening) |
| **Free Cortisone** | 25.66 | 15.5-44.7 µg/g Cr (Night) |
| **Urinary Diurnal Melatonin MT6s** | | |
| **Melatonin** | 50.66 H | 18.0 - 40.9 µg/g Cr (1st Morning) |
| **Melatonin** | 8.80 | 7.3 - 31.9 µg/g Cr (2nd Morning) |
| **Melatonin** | 1.35 | 0.7 - 2.2 µg/g Cr (Evening) |
| **Melatonin** | 3.40 | 1.7 - 11.1 µg/g Cr (Night) |
| **Urinary Creatinine** | | |
| **Creatinine (pooled)** | 0.80 | 0.3-2.0 mg/mL |
| **Creatinine** | 1.32 | 0.3-2.0 mg/mL (1st morning) |
| **Creatinine** | 0.22 L | 0.3-2.0 mg/mL (2nd morning) |
| **Creatinine** | 0.37 | 0.3-2.0 mg/mL (Evening) |
| **Creatinine** | 0.44 | 0.3-2.0 mg/mL (Night) |

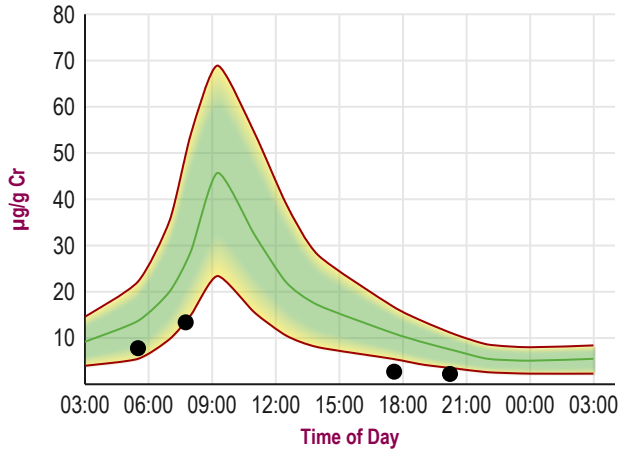
***<dl*** *= Less than the detectable limit of the lab.* ***N/A*** *= Not applicable; 1 or more values used in this calculation is less than the detectable limit.* ***H*** *= High.* ***L*** *= Low.*

## Therapies

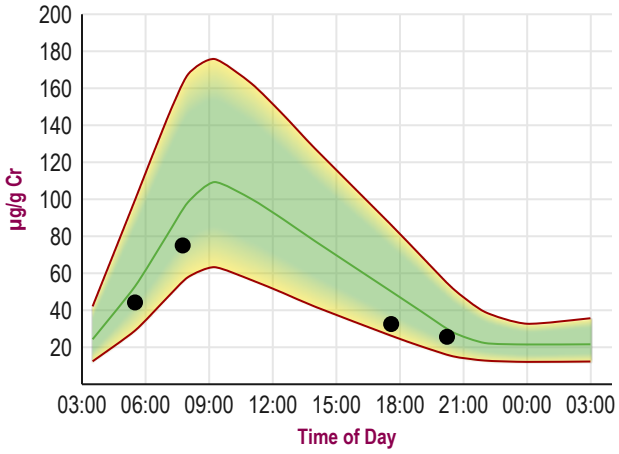
None

## Graphs

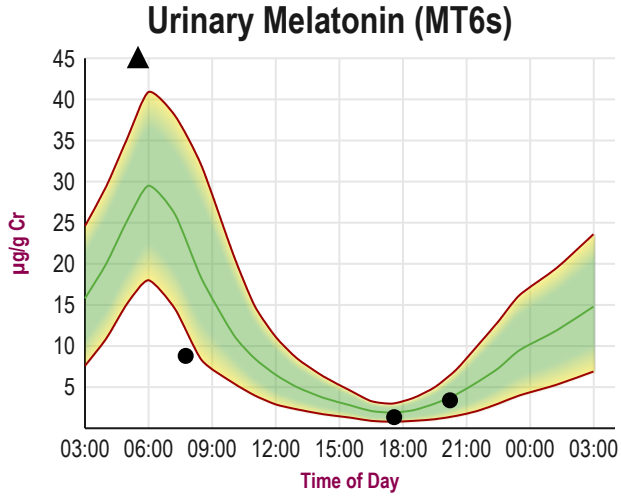
### Urinary Free Cortisol




### Urinary Free Cortisone



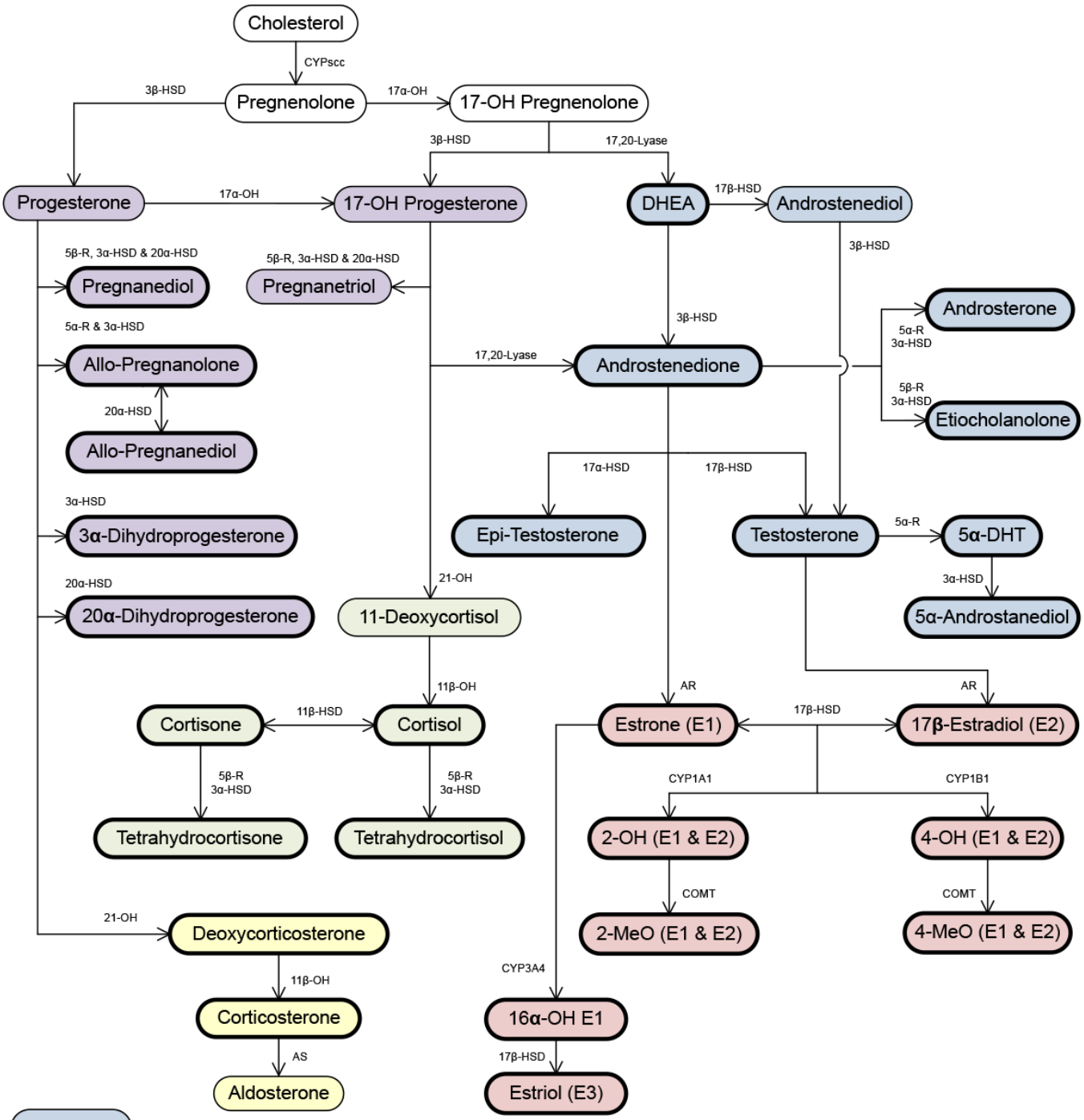

### Urinary Melatonin (MT6s)



| 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

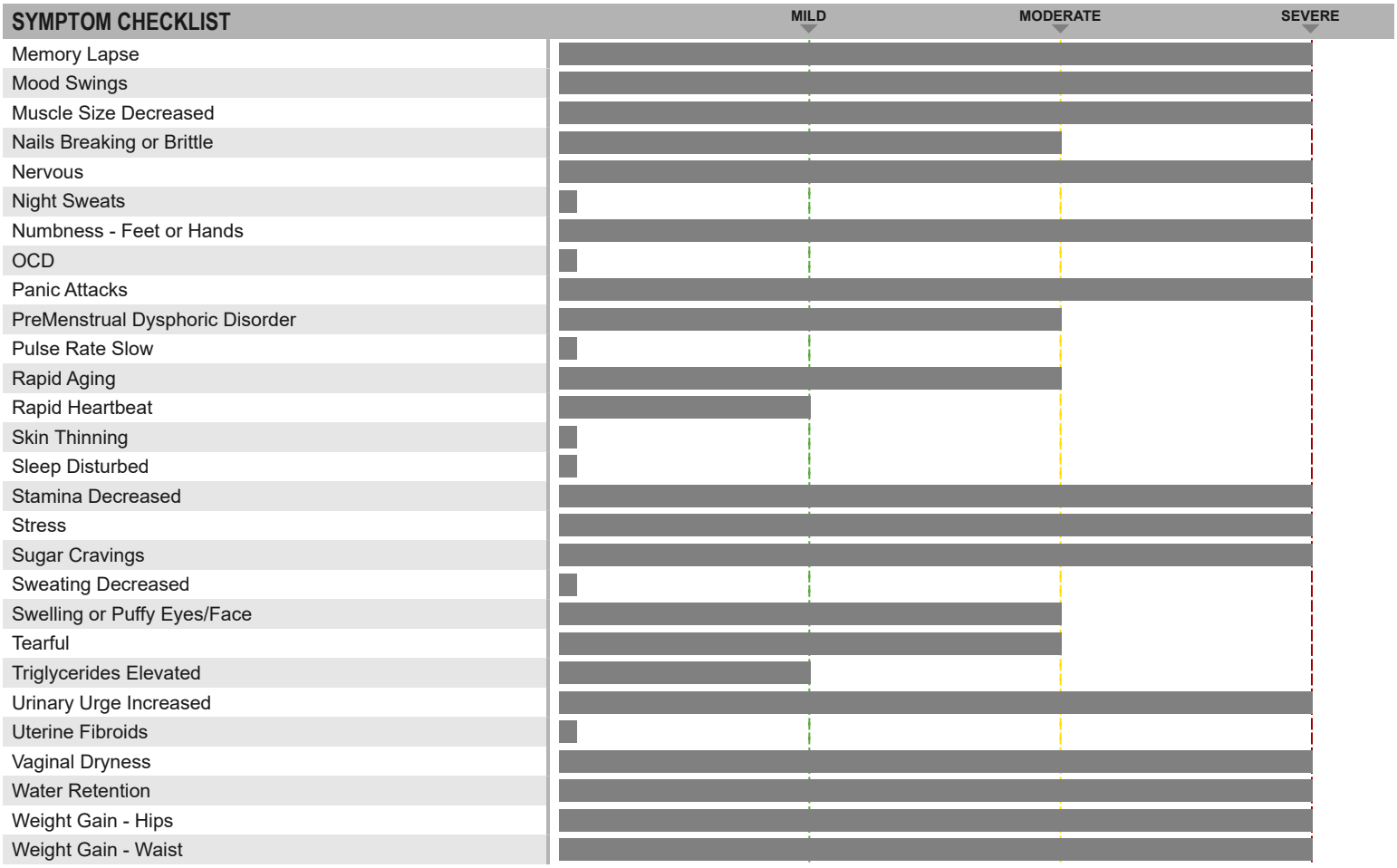



## Enzyme Abbreviations

(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 \| 03/31/25 |
|---|---|
| **Estrogen / Progesterone Deficiency** | 46% |
| **Estrogen Dominance / Progesterone Deficiency** | 61% |
| **Low Androgens (DHEA/Testosterone)** | 74% |
| **High Androgens (DHEA/Testosterone)** | 75% |
| **Low Cortisol** | 63% |
| **High Cortisol** | 54% |
| **Hypometabolism** | 53% |
| **Metabolic Syndrome** | 56% |

| 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)

Estradiol and estrone are within the expected reference ranges for a premenopausal woman. Estriol, on the other hand, is lower than reference range. Low estriol and higher levels of estradiol and estrone, as seen herein, result in a low ratio of estriol to estradiol (E2) + estrone (E1). This indicates low metabolism of estrogens through the estriol pathway, which is considered a safer pathway of estrogen metabolism.

The E3/E2+ E1 ratio originally was based on Professor Henry Lemon's hypothesis (Lemon H. Cancer, 25-2, 423-435, 1970) that estriol, relative to estradiol and estrone, is inert and because of this property is unable to be converted to more dangerous estrogen metabolites (mostly 4-catechol estrogens-see below) that cause DNA mutations and increase risk for breast cancer. According to Lemon, the more estriol, relative to estradiol and estrone, that is present in urine the lower the breast cancer risk. Clinically, Lemon found that Japanese women, who have less breast cancer than women in the US, also have higher E3/E2+E1 ratios. Other scientists attributed this to a higher consumption of green leafy vegetables and iodine in the Japanese diet. Original work suggests that the optimal E3/E2+E1 ratio should be > 1. The ratio of E3/E2+E1 developed at NutriPATH is lower than that proposed by Lemon, and this patient's estriol and ratio of E3/E2+E1 are low based on the NutriPATH reference range.

NutriPATH's E3/E2+E1 reference range is determined by GC-MS/MS and based on the values seen in US women, which are median values of 0.24 ug/g creatinine in premenopausal and 0.29 ug/g creatinine in postmenopausal women NOT using exogenous estrogens. Values higher than the median, and > 1 (usually a result of estriol therapy) are likely more beneficial. In Europe and Japan estriol therapy has been used successfully as a more conservative form of estrogen replacement therapy (mostly for treating vaginal dryness/atrophy) for over 60 years. For references on estriol see: Lee, JR, Zava DT What Your Doctor May Not Tell You About BREAST CANCER: How Hormone Balance Can Help Save Your Life: Chapter 8; Estriol: A Safer Replacement Estrogen.

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 4-hydroxyestrogens (2-MeO-E2, 2-MeO-E1, 4-MeO-E2, 4-MeO-E1) are low or within the lower quadrant of the reference range indicating poor methylation of these hydroxyestrogens. Moreover, the ratios of the more toxic 4-hydroxyestrogens to their methylated forms (i.e. 4-MeO-E2/4-OH-E2 and 4-MeO-E1/4-OH-E1) are low or within low-normal range. 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)

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.

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.

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)

Androsterone is elevated, whereas, etiocholanolone is within normal reference range. Both are downstream metabolites of DHEA and androstenedione (see Steroid Hormone Cascade). Etiocholanolone is created from androstenedione via enzymes 5 beta reductase (5-beta-R) and 3 alpha-hydroxysteroid dehydrogenase (3-alpha-HSD). Androsterone is created from androstenedione via 5 alpha reductase (5-alpha-R) and 3 alpha-HSD. The levels of androsterone and etiocholanolone help determine relative 5 alpha and 5 beta reductase activities. Higher androsterone vs etiocholanolone indicates that the 5-alpha-R dominates. Other downstream metabolites of 5-alpha-R include the androgens dihydrotestosterone (DHT) and 5-alpha androstanediol (Adiol), a neuroactive steroid, as well as the progestogens 5-hydroxyprogesterone (5-HP) and allo-pregnanolone (AlloP), also a neuroactive steroid.

Etiocholanolone 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 and 5 beta reductase, are associated with a lower cancer risk. In contrast to etiocholanolone, higher androsterone indicates higher 5 alpha reductase activity, which increases conversion of T to DHT. Higher levels of DHT may be seen in women with excess androgen levels (T and DHT) and polycystic ovarian syndrome (PCOS).

ANDROGENS AND METABOLITES (TESTOSTERONE, EPI-TESTOSTERONE, AND 5-ALPHA-DIHYDROTESTOSTERONE)

Testosterone (T) and Epi-Testosterone (Epi-T) are higher than the reference ranges for a premenopausal woman. Endogenously, Epi-T and T are synthesized in about equal amounts from androstenedione, a down-stream metabolite of DHEA. With endogenous production, the T/Epi-T

ratio is about 1, and ranges from about 0.5-2. Near equal amounts of T and Epi-T suggest that the T is of endogenous origin, and not from supplementation with DHEA or T. DHT, the down-stream and more potent metabolites of T (DHT binds with 5x affinity to androgen receptors in target cells) is within normal reference range, suggesting lower activity of 5-alpha reductase.

Since T and Epi-T are down stream metabolites of androstenedione and DHEA, a high level of either of these precursors would indicate ovarian (more likely androstenedione) or adrenal (more likely high DHEA) origins of T and Epi-T. In premenopausal women with irregular menstrual cycles a high T associated with a normal to high estradiol, and low luteal progesterone, is commonly associated with PolyCystic Ovarian Syndrome, which is closely linked to insulin resistance and metabolic syndrome. Individuals with high T and irregular menstrual cycles usually also have an elevated LH/FSH ratio (> 3) in blood.

High T, likely of ovarian origin, can also contribute to higher levels of estrogens (E1 and E2) if aromatase levels are high. Higher conversion of T to E1 and E2 may occur selectively in some tissues more than others, contributing to local effects of estrogen dominance (e.g. high conversion in breast tissue leading to fibrocystic breasts). Recent studies have shown that testosterone has a protective effect as regards breast cancer risk (Glaser RL, Maturitas 76: 342-349, 2013) when it is converted to DHT instead of estrogens.

Androgens (T and DHT) 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. Reducing androgen levels, particularly T, below physiological range, can lead to adverse health issues. Excessive levels of androgens often lead to high androgen symptoms such as loss of scalp hair, oily hair and skin, increased facial/body hair, acne, and more aggressive behavior. Birth control pills containing synthetic progestins are often used to suppress the actions of androgens, but often make the cause (insulin resistance/ metabolic syndrome) worse.

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 (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 FREE CORTISONE (E)

Urinary free cortisol (F) levels are lower than reference ranges throughout most of the day, but following a normal circadian rhythm. Cortisone (E) the inert metabolite of cortisol is within normal reference ranges and is following a normal circadian rhythm, indicating adequate synthesis of F, but high conversion to E via 11 beta hydroxysteroid dehydrogenase type 2 (11BHSD2). This would suggest that low cortisol is not likely from low adrenal reserves, as this would result in low synthesis of both F and E. It suggests instead that low F is more likely from normal, or low-normal, cortisol synthesis, but high conversion of F to E by 11BHSD2. High 11BHSD2 may result from use of pharmaceutical medications and hormonal or nutritional supplements.

Lower cortisol levels can be caused by perceived or physical stressors such as emotional/psychological stress (note: stress is self-reported as significantly problematic), sleep deprivation, low protein diet, nutrient deficiencies (particularly low vitamins C and B5), physical insults (surgery, injury, diseases, inflammatory conditions), chemical exposure, low cortisol precursors (pregnenolone, progesterone) or pathogenic infections (bacterial, viral, fungal).

Adequate sleep and rest, gentle exercise, proper diet (adequate protein), natural progesterone, adrenal extracts, herbs, and nutritional

supplements (vitamins C and B5) are some of the natural ways to help support adrenal function. 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 urinary metabolite of melatonin, 6-sulfatoxymelatonin (MT6s), is above normal reference ranges in the first urine void, but returns to levels within expected reference ranges throughout the remainder of the day. Overall, melatonin is following a normal circadian rhythm. Higher melatonin in the first morning void may be normal for this individual (often higher in younger individuals), but may also indicate supplementation with melatonin, a pharmaceutical product that affects melatonin metabolism and clearance, or the use of sleep-inducing herbs the night before collection. Hormone therapies at night might also increase night-time melatonin and result in a higher first morning void.

Melatonin is known to have many beneficial effects in the body. It helps slow the aging process, is a potent anti-oxidant, regulates the immune system, 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, decreases estrogens by inhibiting aromatase, and down-regulates cellular estrogen receptors, which diminishes response of estrogen-sensitive tissues to estrogens). Low melatonin, caused by excessive light exposure during the dark hours, or calcification of the pineal gland caused by aging, 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

Urinary creatinine is within normal reference ranges throughout the day, based on testing diurnal 2x, 4x, or 6x urine collections.
Creatinine values slightly lower than range usually indicate overly dilute urine from excessive water intake shortly before collection, or not spacing collection of multiple urine samples by at least 2 hr (most problematic in second morning urine collection). Creatinine slightly higher than range is usually due to inadequate hydration.
Extreme low or high values may be caused by kidney or other metabolic disorders (e.g. metabolic syndrome and diabetes).